REQUIREMENTS OF VITAMIN A, THIAMINE, RIBOFLAVINE AND NIACIN

Report of a Joint FAO/WHO Expert Group

ROME, ITALY, 6-17 SEPTEMBER 1965

FOOD AND AGRICULTURE ORGANIZATION OF THE UNITED NATIONS

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INTRODUCTION

One of the main tasks of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO) is to advise and assist governments in their attempts to raise the level of nutrition of their peoples. This task can be accomplished to the extent that the most recent knowledge in the science of nutrition can be brought to bear on the problems which the countries, particularly those in the developing regions of the world, have to face. The knowledge of nutritional requirements of populations living under different environmental conditions and with different dietary habits is essential for the evaluation of the existing dietary practices and their influence on the nutritional status of the population, since measures for improvement must be based on the results of such assessment.

FAO and WHO have, over the last two decades, devoted considerable attention to the examination of human requirements of calories and other essential nutrients. FAO convened two committees in 1949 (1) and 1956 (2) to recommend internationally applicable scales of calorie requirements. The recommendations of these committees have been widely applied for the assessment of energy requirements of populations and for the setting up of targets for food production in many countries. FAO and WHO arranged for a review in 1964 of the report of the second FAO Committee on Calorie Requirements. This review (3) indicated that sufficient knowledge had not accumulated in the intervening years to warrant a revision of the recommendations made in 1956.

The situation was quite different, however, with respect to protein requirements which had been first considered by an FAO committee in 1955 (4). Its report stimulated much research and important advances had been made in the knowledge on protein metabolism and requirements since that time. Therefore, FAO and WHO jointly convened an expert group in 1963 to review the question afresh. The report (5) of this expert group indicates a marked change in the approach to the determination of nutritional requirements which is bound to have an influence on the future consideration of requirements of other essential nutrients.

FAO and WHO also convened in 1961 an expert group to consider calcium requirements. The report (6) of this group marked a departure from current concepts of calcium requirements. It stimulated research, the results of which will certainly be useful when the subject of calcium requirements comes up for review in the future.

The time was ripe to consider the question of vitamin requirements also on an international basis. It would probably have been convenient to examine each one of these "accessory food factors" separately. However, the number of vitamins of proved significance in human nutrition was already so large that it would have taken a very long time to complete their consideration in this protracted manner. In view of this, FAO and WHO felt it advisable to consider them in groups. The choice of those to be considered first was determined by two considerations. First, one had to take note of the magnitude of the problem of vitamin deficiencies. The second was the accumulation of sufficient knowledge about the metabolism and functions of some of the vitamins which should provide a justifiable basis for the formulation of requirements. Consequently, vitamin A, thiamine, riboflavine and niacin were chosen. Hence, FAO and WHO jointly convened the present expert group to review the available knowledge on these vitamins and to make recommendations on their requirements.

The group was aware of the large gaps in knowledge which rendered its task difficult. Meager information was available in some important areas, such as the efficiency of utilization of certain vitamin precursors, e.g., β-carotene and metabolism of vitamin A; tryptophan and the factors which influence it, relation between intake and blood levels, and effects of prolonged low and high vitamin intakes on nutriture. However, the group has critically reviewed the available information on these and other relevant aspects of vitamin requirement and has tried to arrive at the best possible estimates under the circumstances.

The group realized that its recommendations can only be tentative and may need reviewing and revision in the future. It was not concerned so much to suggest a set of figures for requirements of individuals. The task was interpreted, in the light of the experience of the earlier expert groups considering requirements of other nutrients, as being to recommend a range and levels of intake which would ensure the health of the large majority of groups of individuals or populations. It is in this context that the report of the group should be viewed and its recommendations interpreted.

1. THE BACKGROUND

Nutritional deficiencies

Nutrition surveys conducted in different parts of the world during the last three decades, and the available hospital records and morbidity and mortality statistics, clearly show that nutritional disorders attributable to deficiencies of vitamin A, thiamine, riboflavine and niacin occur widely in many developing countries. Their incidence and degree of severity vary from country to country, depending upon many factors, some of which are known and some as yet unexplained. These deficiency diseases occur largely among the population groups of low socioeconomic status, usually with defective diets and living in poor sanitary environments which increase the hazards of infection. Poor dietary intake, however, appears to be the principal factor. The summary which follows is intended to indicate the nature and, to a limited extent, the magnitude of the problem, for it must be admitted that reliable figures for the prevalence of these deficiencies are lacking. It should be noted that deficiencies are usually multiple and those which predominate determine the character of the clinical manifestations.

Deficiency of vitamin A

It has long been known that hypovitaminosis A is a frequent occurrence in some countries in South and East Asia. Reports from Indonesia, the Republic of Viet-Nam, Ceylon, Pakistan and India, for example, show that a considerable number of infants and children in the poorest groups of population show clinical evidence of vitamin A deficiency of varying degrees of severity. A more recent survey (7) has revealed the fact that hypovitaminosis A occurs in a large number of developing countries in other parts of the world as well, although to a lesser extent than in South and East Asia.

Deficiency of vitamin A affects mainly the infants and children up to the age of five years, and is often associated with protein-calorie deficiency. The earliest symptom of vitamin A deficiency is night blindness. The most serious clinical manifestation is xerophthalmia which, depending upon the severity of the deficiency, may lead to total or partial blindness. Therefore, hypovitaminosis A is a major cause of preventable blindness in some countries and hence must be considered a serious public health problem.

Thiamine deficiency

Thiamine deficiency, beriberi, occurs essentially in countries in which rice is the main staple food. Its increased incidence with increase in the consumption of polished rice has been amply documented. The region of the world in which it is most frequently encountered is South and East Asia. Reports from the Philippines, the Republic of Viet-Nam, Thailand and Burma indicate that it is still an important public health problem in these countries. Both the cardiac and neuritic types of beriberi are seen in adults. In addition, clinical signs, such as absence of ankle jerks, knee jerks, and the presence of calf tenderness have been recorded in nutrition surveys. These findings suggest the possibility of a moderate deficiency of thiamine existing in the population surveyed.

In infants, the symptoms are different and the disease is more acute and, if untreated, is fatal. A high mortality in infants (2 to 5 months of age) during the period when they are exclusively breast-fed is highly suggestive that the cause is beriberi. This may be due to inadequate thiamine supply to the infant during the period of most rapid growth on account of the low concentrations of thiamine found in the breast milk of mothers in those regions.

Riboflavine deficiency

Clinical manifestations of riboflavine deficiency also occur in South and East Asia and affect individuals at all ages. Unlike beriberi, symptoms and signs of riboflavine deficiency are quite widespread and have been reported from countries in Africa and Latin America. The significance of changes on the lips, buccal mucosa and other mucocutaneous areas, found in nutrition surveys and attributed to riboflavine deficiency, has been a subject of controversy. However, after considering the role of other nutritional as well as nonnutritional factors leading to some

of these changes, and on the basis of successful therapeutic trials, as well as the evidence derived from experimental studies, there seems little doubt that in most surveys the recorded anatomical changes must be largely attributed to a deficiency of riboflavine. Hyporiboflavinosis, even when severe, seldom incapacitates the individual and this may be the reason why not much attention has been devoted to its study and prevention.

Niacin deficiency

The clinical syndrome of pellagra is the classical example of niacin deficiency, although it seldom occurs as a single entity. This is also true of milder degrees of niacin deficiency.

Pellagra is still endemic in some countries of the Near East, Africa and southeast Europe, such as parts of the United Arab Republic, Lesotho, South Africa and Yugoslavia. In most of these, it is associated with diets based on maize, but it is noteworthy that in Central America, where maize is lime-treated, pellagra is rarely reported to occur. On the other hand, niacin deficiency has been reported also in populations not subsisting on maize, such as in India, Cuba and Brazil.

Dietary intakes

The occurrence of clinically manifest deficiencies on a wide scale should make one suspect that a fair proportion of the population in developing countries, particularly that belonging to the low socioeconomic groups, must subsist on intakes of these nutrients not sufficient to protect against nutritional deficiencies. Therefore, it is of importance to consider the habitual diets of various populations.

The group reviewed the results of dietary surveys which have been conducted in various countries. It recognized the limitations of these data since, except for a few countries, surveys have usually been limited with regard to the proportion of the total population covered, the seasons, and the length of time during which the surveys were undertaken. Moreover, even where the average levels of food consumption may appear satisfactory, some deficiencies may occur in the diets of vulnerable groups, such as young children. Despite these shortcomings, the surveys are still the best available sources of information about nutrient intake.

As a background for the discussion of the levels of intake for the vitamins under consideration, the marked contrasts in food consumption

prevailing in different regions and countries of the world were recognized. In North America and western Europe, food consumption is usually high. On the other hand, food consumption is generally low in Asia and the Far East, the Near East, and parts of Africa and Latin America. Although calorie intake is usually satisfactory, periodic shortages of calories are known to be quite serious from time to time in some areas. Diets in these latter regions are generally high in carbohydrates (70 to 90 percent of total calories) and low in fat. Moreover, protein is usually of a comparatively low biological value.

Levels of intake of vitamin A, thiamine, riboflavine and niacin of population groups in various regions as reported in dietary surveys are summarized in Table 1. The figures are given in ranges since conditions differ widely from one country to another and often within the same country.

Some factors affecting vitamin intake

Various socioeconomic factors influence the amount and composition of diets consumed and hence the level of intake of vitamins. Intakes increase with income. Seasonal differences are particularly important since vitamin A intake is generally higher in the spring and summer months due to greater supplies of green leafy and yellow vegetables. Intakes in urban and rural areas also differ in many cases. In general, many rural populations showed higher intakes but in some areas the urban groups may have higher intakes. Ethnic and related cultural factors are also important in determining dietary habits and, therefore, nutrient intakes.

Vitamin A

The majority of data from the various regions indicate that the lowest intakes are found in the Near East as well as in Asia and the Far East (Table 1).

In Latin America and Africa, intakes are generally higher, although much below those observed in Europe and the United States. The wide variation in the nature of the diets in different parts of Africa is responsible for the wide range of values for vitamin A intake. In general, intakes in the arid zones are lower than those in the humid zones.

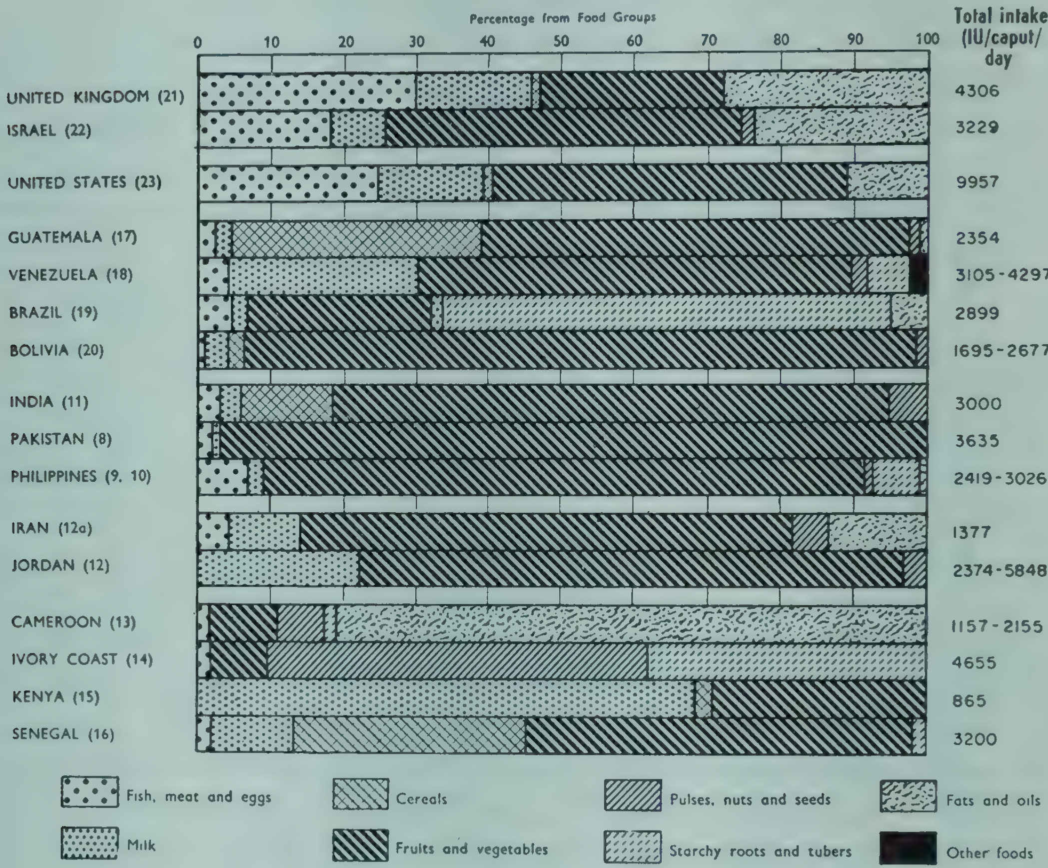
Figure 1 shows that the principal sources of vitamin A in the diets of developing areas are fruits and vegetables — mainly the green leafy and yellow vegetables (65 to 85 percent). However, in some countries in

TABLE 1. – INTAKE LEVELS OF VITAMIN A, THIAMINE, RIBOFLAVINE AND NIACIN OF POPULATION GROUPS IN VARIOUS REGIONS, FROM DIETARY SURVEY DATA [1]

	Vitamin A	Thiamine		Riboflavine		Niacin[2]		Remarks
	IU[3] per caput per day	Milligrams per day per						
		caput	1 000 calories	caput	1 000 calories	caput	1 000 calories	
EUROPE								
Intake, range	1 500–10 000	1.0–2.5	—	0.9–2.1	—	9–24	—	Data from 47 population groups
Intake, majority[4]	3 000– 7 000	1.3–1.8	0.4–0.6	1.0–1.8	0.35–0.73	11–18	4.2–7.8	
UNITED STATES								
Intake average	9 000	2.2	0.48	2.6	0.58	25.5	5.5	*United States Department of Agriculture household food consumption survey 1955.* Report No. 6, 1957
LATIN AMERICA								
Intake, range	1 000–8 000	0.5–2.5	—	0.3–1.8	—	7–22	—	Data from 49 population groups
Intake, majority	1 500–3 000	0.5–1.8	0.30–0.80	0.4–1.0	0.20–0.61	9–18	4.2–10 0	
ASIA AND THE FAR EAST								
Intake, range	400–5 500	0.5–1.5	—	0.3–1.2	—	5–25	—	Data from 91 population groups
Intake, majority	1 000–2 500	0.5–1.0	0.23–0.48	0.3–0.7	0.13–0.40	6–15	2.7–8.6	
NEAR EAST								
Intake, range	400–4 000	0.7–3.5	—	0.3–1.8	—	7–36	—	Data from 76 population groups
Intake, majority	500–2 000	1.5–2.5	0.42–1.0	0.4–1.2	0.15–0.78	12–20	4.4–11.4	
AFRICA								
Intake, range	500–19 500	0.4–3.5	—	0.2–1.4	—	7–24	—	Data from 52 population groups
Intake, majority	1 500– 4 000	0.5–1.8	0.21–1.0	0 5–0.7	0.25–0.65	9–15	4.6–9.5	

[1] Approximately 65 articles and reports on dietary surveys, mainly those conducted since 1955, were reviewed for this purpose. — [2] Preformed niacin only (including bound form). — [3] It is not possible to express these in terms of retinol or β-carotene since in most cases insufficient information is supplied about the sources of vitamin A (1 IU = 0.3 μg retinol or 0.6 μg β-carotene). — [4] "Majority" represents more than 80 percent of the survey data in Asia and Far East, the Near East, Latin America and Europe. In Africa this is only 55 percent.

FIGURE 1. – SOURCES OF VITAMIN A IN THE DIETS OF POPULATION GROUPS SURVEYED IN SOME COUNTRIES



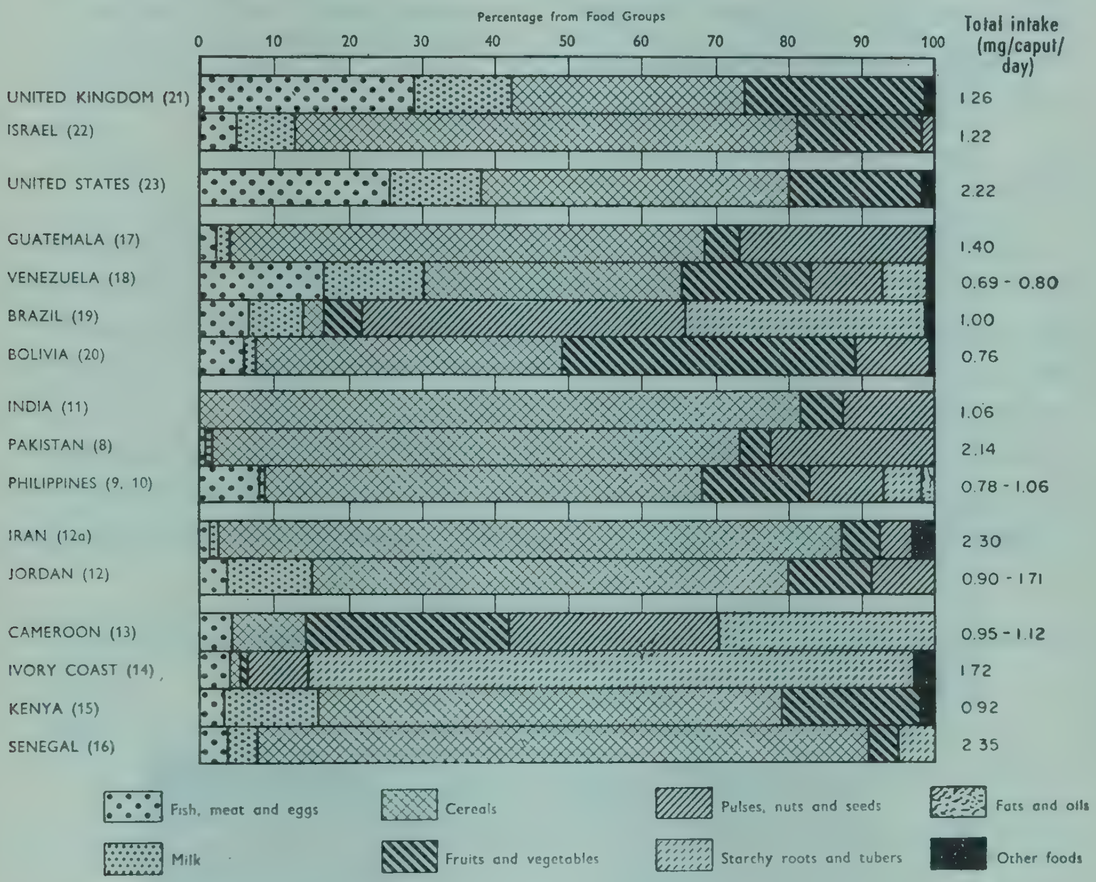
NOTE: Numbers in parentheses in graphs 1 to 4 refer to bibliography.

Africa, the use of red palm oil contributes greatly to the vitamin A intake. The contribution of foods of animal origin to the vitamin A content of diets in many developing countries is low (0 to 20 percent) compared to those in Europe and the United States where this can be as high as 40 percent (8, 23).

THIAMINE

Thiamine intake is lowest in Asia and the Far East where rice is the main staple food (Table 1). However, the intake is influenced by the processing to which rice is subjected before consumption. Parboiled and undermilled rice provide more thiamine than highly milled rice. The intake in Latin America and in the Near East and Africa is generally higher than in Asia and the Far East but lower than in Europe and the United States.

FIGURE 2. – SOURCES OF THIAMINE IN THE DIETS OF POPULATION GROUPS SURVEYED IN SOME COUNTRIES



The principal sources of thiamine in the diet are either cereals or starchy roots and tubers which contribute from 60 to 85 percent of the supply in Asia and the Far East, Africa and the Near East (see Figure 2). In some parts of Latin America, cereals contribute only from 45 to 65 percent, with dried beans and pulses contributing from 15 to 30 percent. In Europe and the United States, cereals provide only about 35 percent, while the contribution of the groups of fruits and vegetables and foods of animal origin is about 20 and 25 percent, respectively.

RIBOFLAVINE

The intake of this nutrient is lowest in Asia and the Far East. In Africa, the Near East and Latin America it is somewhat higher but still much lower than in Europe and the United States. The principal sources of this nutrient in the developing regions are either cereals or starchy

roots and tubers which contribute about 45 percent of the total riboflavine in the diet (Figure 3). In Africa, the fruits and vegetables group or milk may also contribute significant amounts. In Europe and North America the principal source is the group of milk and milk products, while the group of fish, meat and eggs is also important.

Niacin

Consideration of the intake of niacin cannot be dissociated from that of tryptophan intake, as will be discussed later (Chapter 7). Furthermore, the occurrence of unavailable forms of niacin in cereals has to be taken into account. In Figure 4, the contribution of different food groups to the niacin intakes of various countries is shown.

Intakes for niacin are lowest in Asia and the Far East, where rice is the principal source of the nutrient (65 to 85 percent). In Africa, the intake is higher and the principal source may be the local staple food, pulses

FIGURE 3. – SOURCES OF RIBOFLAVINE IN THE DIETS OF POPULATION GROUPS SURVEYED IN SOME COUNTRIES

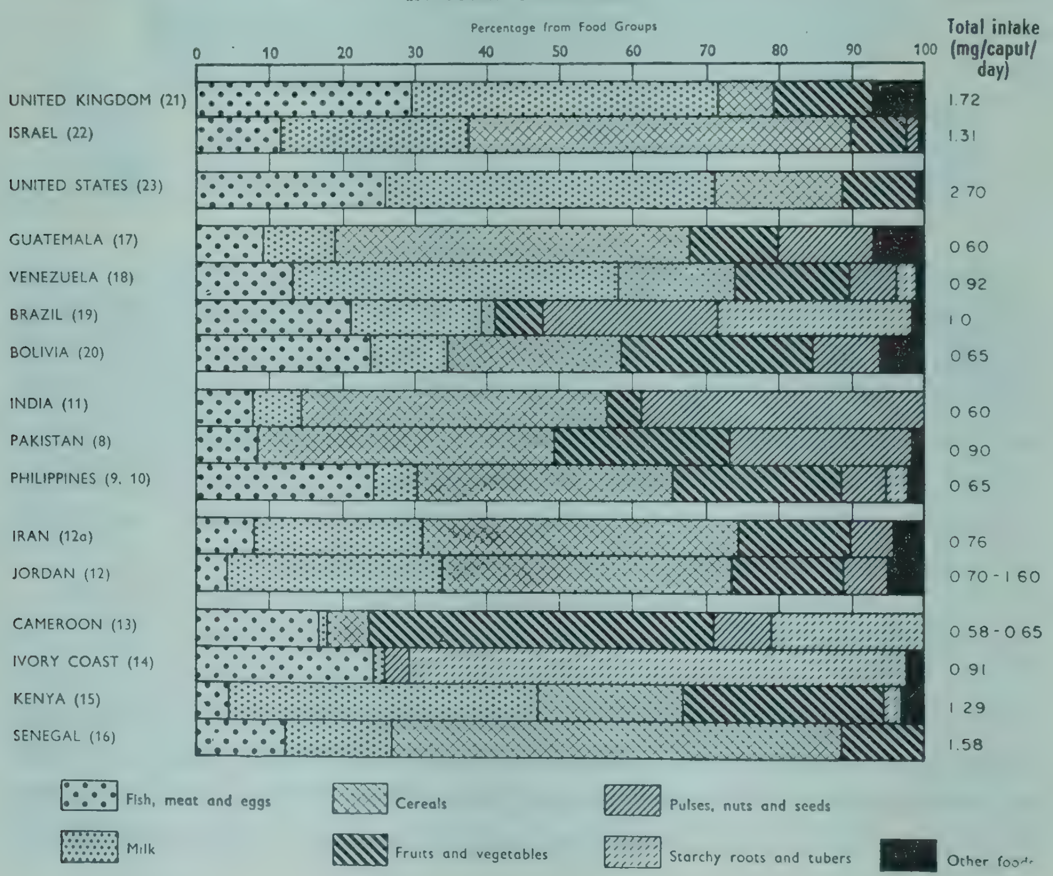
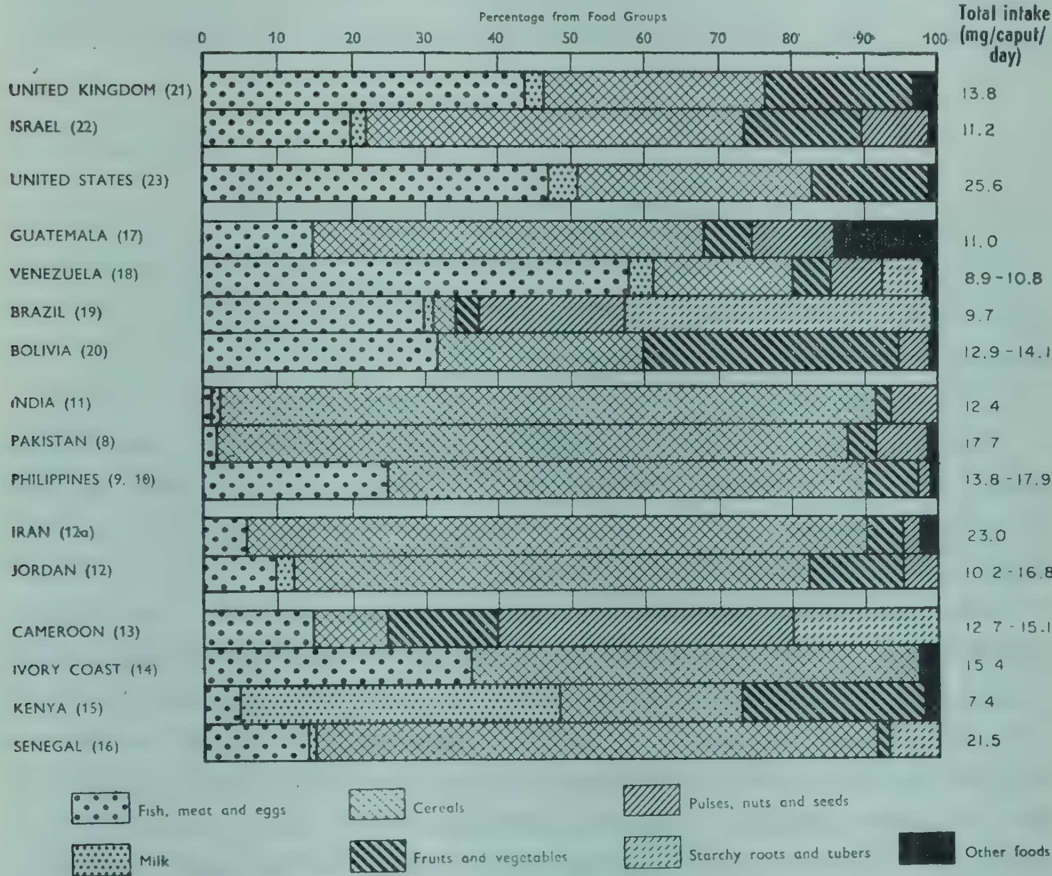


FIGURE 4. – SOURCES OF NIACIN IN THE DIETS OF POPULATION GROUPS SURVEYED IN SOME COUNTRIES



or milk. Intakes are even higher in Latin America and the Near East where, in general, the staple foods are the principal sources of the nutrient. In the United States and Europe, the high levels of niacin in the diet are derived from the group of meat, fish and eggs (30 to 40 percent), cereals (about 30 percent) and the group of fruits and vegetables.

Conclusions

It is clear that there is a great need for more information on the long-term effects of various levels of intake of vitamins on nutritional status. Such information can be obtained by well-co-ordinated studies of dietary intakes and nutritional status of population groups habitually consuming different amounts of vitamins from various foods. The group emphasized the importance of carrying out such studies using modern and standardized methods.

2. BASIC CONCEPTS AND DEFINITIONS

Method of approach to problem

The information used to determine the requirements comes from several sources. Clinical observations of nutritional deficiencies as well as animal research with its greater potential for experimental control have provided much basic information.

After the clinical disorders of vitamin deficiencies were more closely delineated by animal experiments, the needs of man for vitamins were investigated in studies which followed three different approaches. In the first, dietary surveys were conducted in areas where specific nutritional deficiencies existed and the results obtained were compared to those of similar surveys in areas where the population was free of the particular deficiency in question. Comparison of the levels of the specific vitamins consumed by such groups provides a reasonable approximation of the needs of a community. In the second, an attempt was made to determine the physiological parameters of the individual in relation to his nutrient intake. This was done on nutritionally deficient patients as well as on healthy subjects. In the third, an attempt was made to reproduce experimentally some of the signs of clinical deficiencies in groups of volunteer subjects under controlled dietary and environmental conditions and to study the resulting biochemical changes. Such an approach not only permitted the correlation of vitamin intake with the amount needed to present the more obvious pathological changes, but in the case of some of the nutrients, it also provided information on their levels and/or those of their metabolites in the body fluids under controlled dietary conditions. From such information, it was possible to ascertain the intake of a given vitamin which results in the most efficient tissue retention. It also facilitated establishing the level of intake at which the first incontrovertible signs of a vitamin deficiency appeared.

When the results of animal experiments, epidemiological surveys and controlled studies on human subjects all agree, they provide a reasonably good basis for the estimation of the requirement for a vitamin.

Basic concepts

The term " vitamin " is of historic origin and does not reflect the biochemical and physiological mode of action of these nutrients. As knowledge of the functions of vitamins at the tissue and molecular levels accumulates their nomenclature becomes more definitive.

Classification of the vitamins according to their biochemical function distinguishes a category which provides coenzymes, such as thiamine in thiamine pyrophosphate, riboflavine in flavine adenine dinucleotides, and niacin in nicotinamide-adenine dinucleotides. On the other hand, it is well established that, as a constituent of visual pigments, vitamin A functions in the visual cycles. In addition, evidence is accumulating to suggest that it may be necessary for maintaining the structural integrity of membranes in animal tissues.

Those vitamins which supply coenzymes will, at some point of their life cycle in the organism, be substrates of intermediary reactions leading to their incorporation in the prosthetic groups. Consequently, they will undergo, as substrates, a certain amount of wastage, in addition to that encountered during their actual functioning as coenzymes. The accumulation of the vitamin in the body may be influenced by the availability of protein for the building of apoenzymes. This concept, which appears to apply to thiamine, riboflavine and niacin, has made it possible to devise biochemical and physiological tests which assist in the estimation of nutritional requirements.

Definitions

All attempts to deal with nutrient requirements have met with the difficulty of arriving at clear-cut concepts of the amounts of nutrients needed by the body. Thus, a number of terms such as "minimum requirements," "optimum requirement," "recommended allowance" and others have appeared in the literature. Often the terms are ill-defined and may have different meanings for different people. Recognizing this difficulty, the group found it convenient to adopt the following term and

definition for the present report: RECOMMENDED INTAKES. *The recommended intakes for vitamin A, thiamine, riboflavine and niacin are the amounts considered sufficient for the maintenance of health in nearly all people.*

It must be emphasized that the recommended intakes are not expected to cover any additional needs for these vitamins which may result from abnormal conditions such as microbial and parasitic infections, malabsorption syndromes or metabolic abnormalities of genetic or degenerative origin. Nor are they intended to be sufficiently high to meet the requirements under extreme environmental conditions. Furthermore, these recommendations are applicable only when the requirements for calories and all other nutrients are fully met.

The main purposes of the recommended intakes are to evaluate the intakes of population groups, to plan diets and food supplies and to serve as a guide for public health nutrition programs. They are not intended to be used as the sole basis for the evaluation of nutritional status.

3. VITAMIN A

Information about the functions of vitamin A other than its role in vision is still fragmentary. There is no indication that it functions in metabolic systems related to energy production. The weight of available evidence suggests that it functions in the maintenance of subcellular membranes. Previous estimations of vitamin A requirements have been made "per adult man or woman" or per kilogram of body weight. In the absence of convincing evidence that the requirements are more closely related to calorie intake, the group has seen no reason to depart from previous practice.

The metabolism of vitamin A is poorly understood at present. It is known that vitamin A itself is not excreted in urine under normal conditions, and there is not much information on the urinary excretion of its metabolites. Therefore, the criteria of adequacy are restricted to clinical lesions and levels of the vitamin in body tissues and fluids.

Definition of units

There has been confusion in the usage of terms to define the amounts of vitamin A required and ingested in diets. In view of the availability of crystalline vitamin A_1 alcohol (retinol) as a reference standard, the practice of expressing vitamin A values in terms of international units (IU) is no longer necessary or desirable.

In the present monograph, the recommended intakes are described in units of weight and the nomenclature adopted by the International Union of Pure and Applied Chemistry (24) is used. Thus, the term "retinol" is used to mean vitamin A_1 alcohol. The term "vitamin A" will include all compounds having vitamin A activity.

The international unit is equivalent to 0.3 μg retinol (or 0.344 μg

retinyl acetate) or, in the case of the provitamin, to 0.6 μg β-carotene (25). The relative biological activities of the various vitamin A compounds are discussed on page 23. The recommended intakes are stated as micrograms of retinol and a method of adjusting these recommendations for diets containing carotenes is outlined on page 25.

Estimation of requirements

In view of the considerations mentioned in the introduction, there would seem to be only two types of data from which the human requirement for vitamin A might be assessed. There are, firstly, field studies on human population groups in which attempts have been made to correlate clinical evidence of vitamin A deficiency, such as certain changes in retinal rod function and certain signs of the conjunctiva and cornea (26, 27) and/or levels of the vitamin in the blood with dietary intakes of the vitamin. Secondly, there are controlled depletion experiments carried out both on man and on animals of various species, in which the development of clinical manifestations and/or changes in blood vitamin A levels on a certain dietary intake and their abolition by specified increases in intake have been employed in arriving at an estimate of the requirements of vitamin A.

As far as field observations are concerned, considerable information is available from several countries which indicates a very wide range of levels of consumption of vitamin A in diets (see Chapter 1).

In Europe and the United States, where reported intakes are in the range of 3,000 to 9,000 IU[1] per caput per day, vitamin A deficiency is rarely seen. On the other hand, in areas such as Asia and the Far East, where the majority of reported intakes are in the range of 1,000 to 2,500 IU,[1] clinical vitamin A deficiency is known to occur in parts of the population. However, there is little information that can be utilized to define the quantity of vitamin A required to maintain health.

Several human deprivation and recovery studies on adult volunteers have employed the detection of impairment of retinal rod function as a criterion of adequacy. These studies have been reviewed elsewhere (28, 29). Of these, the Sheffield experiment (28) is considered to be the best controlled, although recovery was studied in only three subjects; in each case

[1] The original surveys do not supply data relating to the actual intake of carotene and retinol derivatives, hence the international unit has been employed in this instance.

a different type of treatment was instituted. The correction of defective dark adaptation and the restoration of rod scotometry patterns to those found in well-nourished persons were accomplished with a dose of 390 μg retinol (about 6 μg/kg) per day. In general, the other human studies support the results of the Sheffield experiment.

A number of studies on the cow, sheep, pig (30) and horse (31) have been conducted, usually with young animals. The clinical assessment of deficiency was crude. Animals were maintained on diets low in vitamin A until they developed night blindness, as indicated by their inability to avoid obstacles in semidarkness. The results obtained with therapy indicated a requirement of between 4 and 6 μg retinol per kilogram of body weight per day for these species. Although direct extrapolation to the human is not possible, these findings lend support to the figure derived from the Sheffield experiment.

The group accepts the figure of 390 μg retinol per day as approximately the intake required to prevent visual symptoms of vitamin A deficiency in the adult. However, it was not possible to determine whether liver storage of vitamin A occurred at this intake. It was noted (28) that the 390 μg dose level of retinol was not sufficient to return the blood vitamin A level to that found before the initiation of depletion.

There is much evidence, derived from animal studies, that a somewhat complicated relationship exists between the serum level of vitamin A and its deposition in the liver. It is widely accepted that serum levels are maintained at the expense of liver reserves when intake is low. It has been shown (32) that in rats given a range of oral doses of retinol, plasma vitamin A levels increased with dosage but liver storage did not occur until the plasma concentration was nearly maximal. This has been confirmed in other types of experiments (33).

Although it was not possible to determine if any liver storage occurred in the subjects of the Sheffield experiment (28), in view of this evidence it seems that 390 μg retinol per day, which was found sufficient for the alleviation of visual symptoms, may be inadequate to maintain liver stores in an adult, and that a higher intake should be recommended.

Information relating the dietary intake of vitamin A to the levels of the vitamin in blood and/or liver might be of value in estimating requirements. Reports of a large number of nutrition surveys (34) providing data on vitamin A intakes and serum levels of population groups were examined. However, it was not possible to determine the level of intake

that might be associated with satisfactory serum levels. Similarly, data reviewed elsewhere (29, 35) relating to vitamin A in the liver gave little information about previous vitamin intakes, and was of no value for the present purpose.

In the Sheffield experiment (28) an intake of 750 μg retinol per day for 14 to 17 months was sufficient to prevent development of any impairment of dark adaptation and to maintain plasma vitamin A levels constant in two individuals. When the intake was increased to 1,500 μg retinol per day there was no change in plasma vitamin A. It was also noted in this experiment that the dosing of one of the depleted subjects with 1,500 μg β-carotene per day produced an almost immediate recovery from visual defects and restored blood vitamin A to the predepletion level within three weeks; a second subject responded more slowly. As discussed below (page 23), this dosage of carotene would make less than 750 μg retinol available to the body.

In view of the above considerations and realizing the limitations set by the paucity of information available and the difficulty of extrapolating findings from experimental animals to man, and recognizing the desirability of maintenance of a liver reserve of vitamin A, and bearing in mind the need to take into account the factor of individual variation, *the group adopted a recommended intake of 750 μg retinol per day for the normal adult.*

Adults

The recommended intake for adults of both sexes is 750 μg retinol per day. Adjustments of this recommendation for pregnancy and lactation are discussed below.

Pregnancy

From limited autopsy data (29), it appears that the liver of the newborn infant contains sometimes as much as 45 μg retinol per gram of tissue. The liver at birth weighs about 120 to 160 g (36) and therefore contains as much as 5,400 to 7,200 μg retinol. In order to deposit this amount in the fetus, the maternal stores would be drawn upon to the extent of about 25 μg retinol per day throughout the duration of pregnancy.

This figure would be increased by the quite unknown but probably limited additional amounts resulting from any inefficiency in transfer across the placenta, from the metabolic needs of the fetus, and from maternal tissue growth. Assuming that the habitual diet of the woman provides 750 μg retinol per day, the increase in total daily requirement associated with pregnancy can be met without increasing the recommended intake for the adult. *The recommended intake during pregnancy is 750 μg retinol per day.*

Lactation

Information on the volume of milk secreted at various stages of lactation is meager. However, the WHO Expert Committee on Nutrition in Pregnancy and Lactation (37) accepted an average milk yield of 850 ml per day, with a retinol content of 49 μg/100 ml in a well-nourished population. The additional needs for lactation must be at least as great as the vitamin A secreted in the milk. *The recommended intake during lactation then is 1,200 μg retinol per day.*

Infants and children

For infants from birth to 5 months, it is assumed that exclusive breast feeding can provide sufficient vitamin A to maintain health, permit normal growth, and allow storage of the vitamin in the liver.

In the absence of direct evidence, the recommended intakes for infants and children have been calculated in relation to the estimated vitamin A intake of breast-fed babies and the recommended intake for adults.

From animal studies, it is now well established that during growth the vitamin A requirement is increased (38). It has been assumed that the vitamin A requirement of children is related to the rate at which body weight is increasing in proportion to body size. The group has adopted this concept as an approach to obtaining a first approximation of the requirement.

The WHO Expert Committee on Nutrition in Pregnancy and Lactation (37) considered that adequacy of lactation could best be judged by satisfactory growth of the infant during the period when it is exclusively

breast-fed. Under such conditions, "a gain of 800 g ± 20 percent per month during the first six months of life or the doubling of the birth weight by about the end of the fourth month of life may be regarded as satisfactory." Assuming an average milk yield of 850 ml per day (2) and a retinol content of 49 μg/100 ml breast milk in a well-nourished population (37), satisfactory breast feeding would give a total of 420 μg retinol per day during the first five or six months.

The average birth weight of an infant in well-nourished communities of Europe and the United States is about 3.3 kg and, with satisfactory growth, its weight at the end of 3 and 5 months would be 5.7 and 7.3 kg, respectively. At these ages, retinol in breast milk is estimated to provide 66 and 52 μg retinol/kg body weight, respectively (Table 2).

TABLE 2. – ESTIMATED INTAKES OF RETINOL IN BREAST-FED BABIES

	Age	
	End of 3 months	End of 5 months
WESTERN EUROPE AND UNITED STATES		
Weight (kg)	5.7	7.3
Intake (μg/day)	420	420
Intake (μg/kg)	66	52
INDIA		
Weight (kg)	4.7	6.1
Intake (μg/day)	187	187
Intake (μg/kg)	40	30
JORDAN		
Weight (kg)	5.7	7.3
Intake (μg/day)	128	128
Intake (μg/kg)	22	18

In some areas of the world, retinol levels in milk are below that described above; thus, certain observations in India (39) and Jordan (40) yield average values of 22 and 15 μg retinol per 100 ml, respectively. It is an accepted fact that under these conditions an exclusively breast-fed baby has a normal rate of growth during the first five months of age, showing that lactation has been adequate for growth. Since the average birth

weight in India in the lower socioeconomic groups is of the order of 2.7 kg (37), the weight at the end of 3 and 5 months can be estimated at 4.7 and 6.1 kg and the retinol intake at 40 and 30 μg retinol per kilogram. With the still lower vitamin A concentration in breast milk in Jordan and a reported birth weight of 3.3 kg (41), the estimated intakes of retinol at the end of 3 and 5 months would be 22 and 18 μg retinol per kilogram per day, respectively (Table 2).

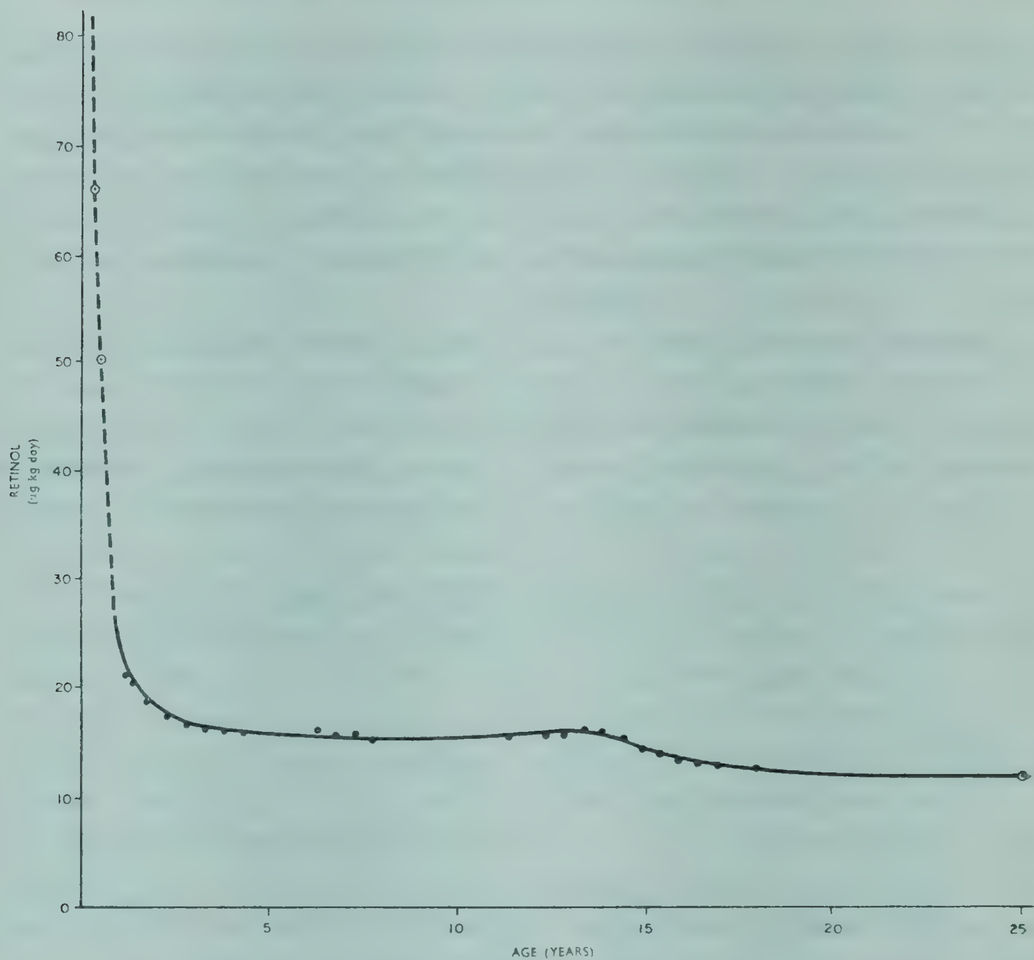
It can be seen that there is a wide range of retinol intakes in breast-fed infants over which satisfactory growth might occur during the first six months. No information is available about liver stores of the vitamin in these infants. However, in both India and Jordan, clinical vitamin A deficiency is common in children of the lower socioeconomic groups below the age of 5 years (7). The clinical manifestations of vitamin A deficiency are seldom, if ever, seen in infants and young children who have been breast-fed during the first six months in the United States or Europe. It is concluded that, whereas the lower levels of retinol intake (18 and 30 μg/kg at the end of 5 months) may be adequate for growth, they are probably insufficient to promote a significant degree of liver storage.

It has been reported (42) that an intake of 7.5 μg/kg body weight by artificially fed infants of 3 to 12 months of age prevented impairment of dark adaptation. However, interpretation is difficult since earlier breast or artificial feeding would have significantly affected liver reserves and hence time required for depletion. Furthermore, data presented in Table 2 and discussed in the text above suggest that even higher levels of retinol intake, as would be obtained in India and Jordan, may be insufficient to provide adequate liver reserves. It seems probable that the true requirement of the infant for vitamin A lies between 200 and 420 μg retinol per day.

The group concludes that recommended intakes of retinol at the end of 3 and 5 months of life should be 420 μg per day or about 65 and 50 μg/kg per day, respectively. The recommended intake for the adult may be calculated as 12 μg/kg. To join these points in Figure 5, a curve, based on body weight increment per kilogram of body weight at various ages, derived from reported data (36) has been fitted. From this curve, an approximation of the recommended intake of retinol per kilogram of body weight per day at various ages has been obtained. *The recommended intakes of retinol per day are shown in Table 3.*

No further adjustment in recommended intakes need be made for differences in body weight within the age groups shown in the table.

FIGURE 5. – BASIS FOR ESTIMATION OF RECOMMENDED INTAKES FOR CHILDREN[1]



[1] Curve is based on the body weight increment/body weight calculated from reported data (36).

TABLE 3. – RECOMMENDED INTAKE OF RETINOL AT VARIOUS AGES

Age	Recommended intake µg retinol per day	Age	Recommended intake µg retinol per day
0-6 months	[1]	7-9 years	400
6-12 "	300	10-12 "	575
1 year	250	13-15 " . . . . . . (boys-girls)	725
2 years	250		
3 "	250	16-19 years . . . . . . (boys-girls)	750
4-6 "	300	Adults (man-woman) .	750

NOTE: For diets containing both carotene and retinol, adjustment must be made as described on page 25.

[1] For infants 0 to 6 months, it is accepted that breast feeding by a well-nourished mother is the best way to satisfy the nutritional requirements for vitamin A.

Factors affecting requirement

Physical activity

There does not appear to be any evidence that requirements for vitamin A are influenced by physical activity.

Climate

No data are available regarding the effect of climatic factors on the vitamin A requirements in man. It has been reported (43) that vitamin A-deficient animals have an impaired resistance to cold, that the deficiency state can be more rapidly induced in a hot environment, and that high temperatures can be better tolerated after massive doses of the vitamin. However, others (44) could detect no significant effect of temperature on the storage of vitamin A in the liver of the rat. It is considered that such evidence as is available at present does not warrant any specific recommendations in relation to climate.

Pathological states

In every environment where vitamin A deficiency is a problem, the relationship to other pathological conditions is important. Xerophthalmia is associated with protein-calorie deficiency diseases and with infectious diseases. Their public health significance is mentioned in a later section of the present report. Any pathological condition which interferes with fat absorption is likely to interfere with vitamin A absorption.

Factors affecting the availability and utilization of vitamin A in foods

Efficiency of utilization of β-carotene

The major source of vitamin A in most diets is β-carotene (see Figure 1); few, if any, natural diets contain exclusively retinol. Therefore, it is of practical importance to recognize that β-carotene is not utilized as efficiently as retinol by the human body.

In the rat, under conditions of suboptimal intake, it is well established

that 1 μg retinol has the same biological activity as 2 μg β-carotene (26, 29). Provided that only the "absorbed" carotene (see below) is considered, approximately the same relationship appears to hold for the human at suboptimal intakes. Thus, in the Sheffield experiment the visual defects were cured by 390 μg retinol or by 960 μg "absorbed" β-carotene; and hence, 1 μg retinol was found to be equivalent to about 2.5 μg "absorbed" β-carotene. In the light of this study and of the known relationship in the rat, it is assumed that about 50 percent of the β-carotene "absorbed" from the diet can be transformed into retinol. This may be considered as the efficiency of conversion.

A number of investigators have studied the availability of carotenes in foods. The technique has usually been that of a balance study, i.e., the carotene excreted in the feces has been expressed as a percentage of the carotene intake, and the difference is presumed to represent the carotene "absorbed."

While this approach may be subject to error (e.g., there is no account taken of carotene destruction), it is important to realize that these factors also operated in the Sheffield experiment where the basic efficiency of conversion for the human was estimated. Therefore, it is reasonable to examine the "apparent absorption" as reported in the literature. Data from a number of human experiments are summarized in Appendix 3.

Only a limited range of foods has been examined. It is not possible to make an accurate prediction of the availability of carotene from these studies. The data are too few and variable, even within a single study. Further, it is probable that most of the methods of determination included both α- and β-carotene and, in the case of the early methods, perhaps some of the other carotenoids. The proportion of carotenoids other than β-carotene varies.

In view of these difficulties, the best approximation for availability of carotenes in diets is 33 percent. This underestimates the availability in some foods and overestimates it in others.

The group recommends that, in the absence of more specific data for foods, the availability of β-*carotene be taken as one third and that the efficiency of conversion in the body be accepted as one half of the available* β-*carotene: hence the utilization efficiency in the human is taken as one sixth. Thus, in the human, 1* μg β-*carotene in the diet is taken to have the same biological activity as 0.167* μg *retinol.*

Modification of recommended intake for diets containing carotenes

Human diets contain both retinol and carotenes in widely varying proportions, as can be seen from Figure 1. It may be desirable to adjust the recommended intake in accordance with the biological activity of the vitamin A compounds in the diet as shown below:

$$\text{Recommended intake of mixed vitamin A-active compounds} = \frac{\text{Recommended intake of retinol}}{0.167\ k + (1-k)}$$

where k = proportion of β-carotene in diet[2]

$$= \frac{\beta\text{-carotene }(\mu g)}{\beta\text{-carotene }(\mu g) + \text{retinol }(\mu g)}$$

Some examples of its application to various dietaries are shown in Table 7, Chapter 9. The derivation of the above equation is explained in Appendix 4.

Carotenoids other than β-carotene

Of the carotenoids, β-carotene has the highest biological activity. The activity of other carotenoids varies, some having no activity and others about 50 percent of that of β-carotene.

The group agreed with the suggestion (46) that the activity of other total mixed carotenoids (with vitamin A activity) be taken as one half of that of β-carotene.

Retinol

After the oral administration of retinol to rats, as much as 80 percent can be recovered in the liver and kidneys (the efficiency depends on the dosage) (29). No data on humans are available.

The retinyl esters appear to be utilized as efficiently as retinol itself if compared on the basis of their retinol content.

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[2] Provitamin A. It is assumed in the report that other naturally occurring vitamin A-active carotenoids will be included quantitatively on the basis that they have one half of the biological activity of β-carotene.

Dehydroretinol

While retinol is the predominant source of preformed vitamin A for humans, dehydroretinol (vitamin A_2) is known to occur in fish liver oils. Usually the livers of saltwater fish contain mostly vitamin A_1 with only small amounts of vitamin A_2. Livers of freshwater fish, on the other hand, contain higher proportions of vitamin A_2 and in some Indian fish it has been found to be almost the only component (45). The biological activity of dehydroretinol is only about 40 percent of that of retinol in rat growth tests (88). In spite of the absence of definite data for the human, it may be necessary to recognize the low biological activity of dehydroretinol in areas where freshwater fish form a major source of vitamin A.

Factors affecting the vitamin A value of foods

Dietary fat and natural antioxidants

Dietary fat has a negligible effect upon the utilization of retinol unless rancid oils or oils rich in polyunsaturated fatty acids are present in the diet in sufficient quantity to induce retinol destruction. In this regard, natural antioxidants such as α-tocopherol (29, 47) and ascorbic acid (48) may exert a protective effect on carotene and retinol.

The addition of fat to a fat-free diet or to one very low in fat may improve the availability of carotenes (see data in Appendix 3, for example). While this may be of significance in very low fat diets, the group doubted whether it was of significance in most human dietaries.

Dietary protein

The group is not aware of any evidence that the quality or, within the normal range of protein intake of the human, the quantity of protein exerts any significant effect on utilization of vitamin A, provided that protein requirements are met.

Inadequate protein intake has an adverse effect on the efficiency of intestinal absorption of retinol, its transport in blood and its metabolism (49). In the case of carotene, protein deficiency markedly depresses the intestinal conversion of β-carotene to retinol derivatives (50, 51). Thus, the effect is more profound than in the case of retinol. These observations, which have been made mostly on experimental animals, have been

confirmed to a certain extent in children with protein-calorie deficiency diseases (52-54).

In those environments where protein-calorie deficiency is frequently observed, carotenes usually form the major source of vitamin A in the diet. If the observation, made on experimental animals, that protein deficiency impairs carotene utilization, is confirmed by further observations in humans, there are obvious implications. Therefore, problems of meeting vitamin A and protein requirements under such conditions should be considered together.

Processing and preservation of foods

β-carotene is present as a lipoprotein complex in all the green parts of plants. It is found in abundance in red palm oil, carrots, green peppers, spinach and other green leaves. Retinol occurs widely in animal tissues, principally in the liver (e.g., fish liver oils). The offals, butter and eggs constitute good dietary sources of vitamin A provided the animals from which they are derived are appropriately fed. Lean meat and lean fish are almost devoid of vitamin A.

Vitamin A is relatively stable to heat but sensitive to oxidation. The destruction of retinol and carotenes is accelerated by the process of autooxidation under the influence of light. Vitamin A is also considered to be sensitive to ionizing radiation, although it is not known with certainty whether these destroy the vitamin directly or through the action of other products formed during irradiation. It seems that the medium in which vitamin A is incorporated influences the level of destruction caused by ionizing radiation.

The modern techniques of industrial processing of milk (pasteurization, sterilization, concentration, dehydration) cause only a very slight loss of vitamin A. Similarly, canning also causes little loss. No carotene remains in refined edible oils.

The extent to which vitamin A is destroyed in domestic cooking varies greatly depending upon several factors, such as temperature, duration, presence of moisture and exposure to light and air, and the pH of the medium.

As is apparent from Appendix 3, the degree of cellular rupture appears to be of major importance in rendering carotenes available. Thus, the carotene of carrot puree is used more efficiently than that of carrots cooked in larger pieces and much more efficiently than that of raw carrots.

4. THIAMINE, RIBOFLAVINE AND NIACIN

Bases for expressing the requirements

In view of the well-recognized roles of thiamine, riboflavine and niacin in energy metabolism, it is reasonable to relate their requirements to energy expenditure. Therefore, the requirements are considered in terms of milligrams per 1,000 calories. It is assumed that the individual is in calorie balance because it is only under this condition that energy expenditure and calorie intake are equal.

Variation among individuals

The minimum requirement of thiamine, riboflavine or niacin was considered to be the level of intake of the vitamin which would be just sufficient to prevent the appearance of clinical or biochemical lesions, or both.

When recommended intakes based on these requirements are being designed for groups of people, it is necessary to recognize that there is biological variation among individuals. An estimate of this biological variation may be obtained from the known variation pertaining to basal energy expenditure (BMR). The same assumption was made with regard to proteins by the Joint FAO/WHO Expert Group on Protein Requirements (5). From data on the BMR in adult men (55), the standard deviation has been found to be about 10 percent of the mean. In the absence of any more precise measures of the variation in individual vitamin requirements for thiamine, riboflavine and niacin, it was considered that 20 percent is a reasonable approximation to two standard deviations covering about 97.5 percent of the population. An estimate of the minimum requirements for these vitamins has been obtained from a number of studies, as explained in the corresponding chapters in this report (Chapters 5,

6, 7). It is anticipated that the addition of 20 percent to these estimates to arrive at the recommended intakes of thiamine, riboflavine and niacin will ensure that, by adhering to these recommendations, the needs of "nearly all people" for these vitamins will be met.

Growth, pregnancy and lactation

In general, there is little evidence that the recommended intakes of thiamine, riboflavine and niacin expressed per 1,000 calories should differ for children and adults.

For infants up to 6 months, it is considered that breast feeding by a well-nourished mother is the best way to satisfy the needs for these vitamins, even though the amount of the vitamins per 1,000 calories may differ from that recommended for adults.

The group agrees with the WHO *Report on nutrition in pregnancy and lactation* (37) that, insofar as thiamine, riboflavine and niacin are concerned, it is not possible to give any precise indication of the physiological cost of pregnancy and lactation. It is recommended, therefore, that in general the practice of relating intakes of thiamine, riboflavine and niacin to calorie requirements should be followed during pregnancy and lactation.

Mental activity

Some work on experimental animals indicated a possible effect of vitamins of the B complex on higher nervous activity (144). It has been suggested that supplementation of diets with thiamine, riboflavine and niacin may contribute to an improved performance in subjects engaged in stressful mental activity. The significance of such observations in terms of the effect on mental activity and of stress in augmenting requirements of these vitamins needs to be evaluated by further research.

5. THIAMINE

Considerable information is available concerning the role of thiamine in intermediary metabolism. Thiamine as the biologically active thiamine pyrophosphate (diphosphothiamine, cocarboxylase) has an important role in carbohydrate metabolism as a coenzyme in such reactions as the decarboxylation of α-keto acids, particularly of pyruvate and α-ketoglutarate. In thiamine deficiency, pyruvic and lactic acids tend to accumulate in the tissues and body fluids. Thiamine pyrophosphate also functions as a coenzyme in the "transketolase system" associated with the direct oxidative pathway of glucose metabolism. This system provides a source of ribose for the formation of nucleotides, including nicotinamide adenine dinucleotide phosphate for various functions. Thiamine does not appear to be stored in the body to any appreciable extent; consequently, deficiency symptoms may be observed within a few weeks in subjects maintained on a deficient diet.

Excess ingested thiamine appears in the urine but a quantity of the vitamin is metabolized and the metabolites are also excreted in the urine. The nature of the metabolites is only partially understood but they are numerous and include those derived from the thiazole and pyrimidine moieties of the vitamin.

Principles and methods of estimating requirements

Several approaches have been considered in the determination of the minimum requirement for thiamine (56, 57). The principal ones are the following:

1. The urinary excretion decreases proportionately to thiamine intake to a critical point, after which further lowering of intake results in only minor changes in urinary excretion. It is assumed that the thia-

mine intake at this critical point represents the minimal intake which will maintain a physiologically adequate thiamine concentration within the tissue. Intakes above the critical point result in less efficient retention of thiamine in the tissues (58-63).

2. Related to the above procedure are the so-called "dose-retention tests." The tests are conducted by the administration of a dose of thiamine orally or parenterally followed by the determination of the percent of the dose excreted into the urine during the subsequent 4 or 24 hours. The values obtained are considered to indicate the extent of saturation of the tissues with thiamine (58-60, 64).

3. Another approach is based on the measurement of the urinary excretion of the metabolites of thiamine, principally the pyrimidine and thiazole moieties, as an indication of the amount of thiamine utilized and requiring replacement (65, 66).

4. The appearance of abnormalities in carbohydrate metabolism has also been investigated with respect to thiamine intake. These abnormalities are judged mainly by alterations in the concentration of lactate and pyruvate in the blood or urine, and are particularly useful when the involved metabolic pathways are subjected to a metabolic stress, such as load of glucose plus physical exercise (56, 59, 67). Erythrocyte analysis for "transketolase activity" (66, 68) and other tests for thiamine pyrophosphate (69, 70) have also been employed in the estimation of thiamine requirements.

5. The appearance and disappearance of clinical signs in controlled experiments in relation to known intakes of thiamine have also proved useful (59).

6. Suggestive information concerning thiamine requirements has been obtained from epidemiological findings and nutrition surveys (34, 60, 71).

Several independent groups of investigators have determined the minimum daily requirement of thiamine for men using either one or a combination of the above criteria in a comprehensive approach. The criteria under (1), (3) and (4) have been most useful in the formulation of the recommended intake for thiamine.

Estimates of requirements

It has been the general practice to express the requirements for thiamine per 1,000 calories ingested. A review and analysis of available evidence reveal that values for thiamine intake ranging between 0.2 and 0.5 mg per 1,000 calories have been reported as those needed to satisfy "requirements" (59, 65, 66, 74-79). These large differences are explained by differences in approach and in experimental procedures used to estimate thiamine requirements.

Excretions of from 5 to 20 μg thiamine per day have been associated with thiamine intakes of about 0.2 mg per 1,000 calories (60-63). In cases of beriberi, excretion of 0 to about 15 μg has been observed (57).

In the Minnesota studies (80), it was concluded that "for the period studied, no benefit of any kind was observed to be produced by an intake of more than 0.23 mg of thiamine per 1,000 calories." Since their observation period lasted only 10 to 12 weeks, the authors drew no conclusions about the requirement for longer periods of time. In another carefully conducted study in adult men (Elgin studies) in which levels of thiamine in this low range were evaluated by comprehensive criteria, it was concluded (59) that 0.40 mg thiamine per day was below the minimal requirement for their subjects who were consuming about 2,000 calories per day, or about 0.20 mg thiamine per 1,000 calories.

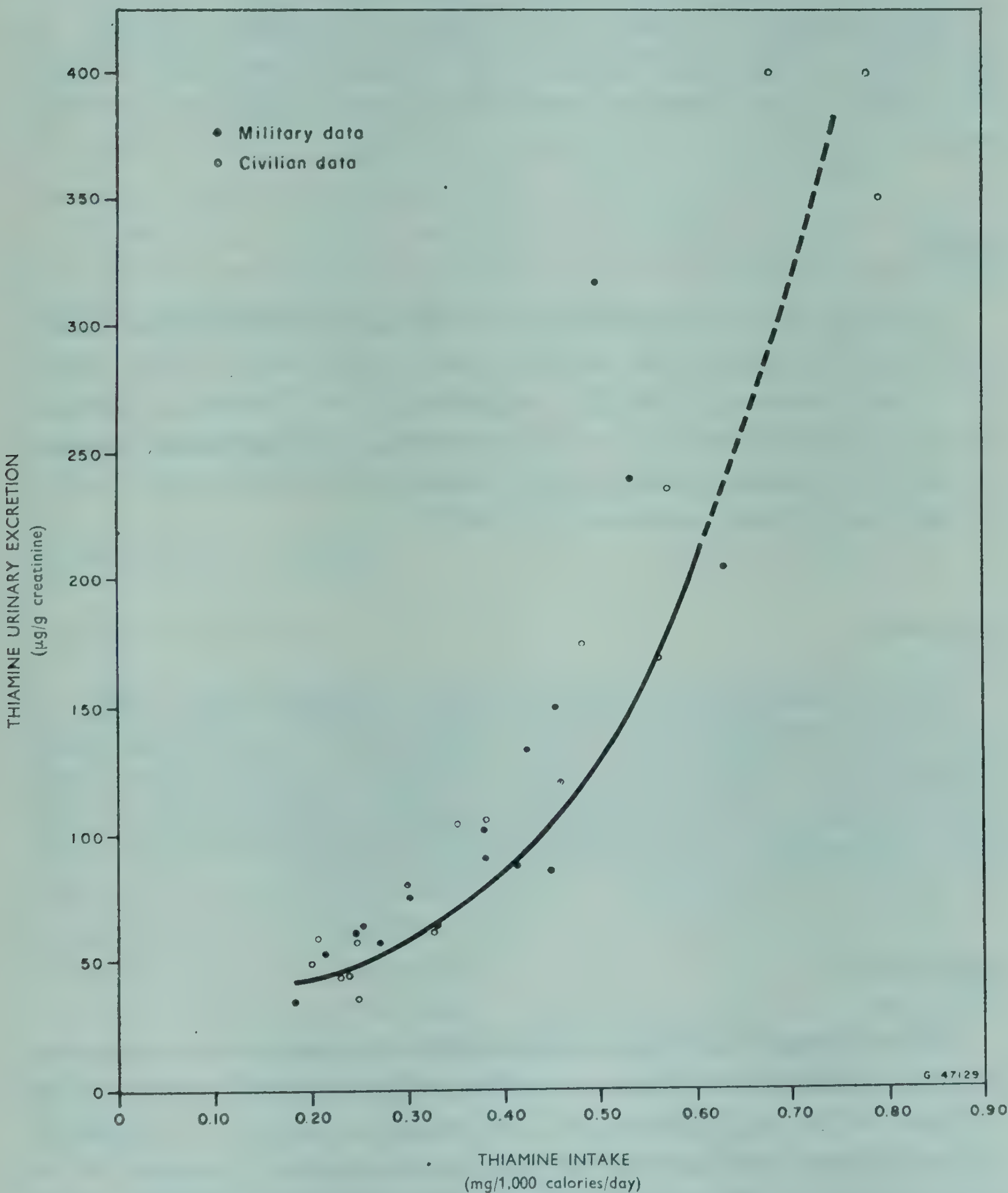
It has been observed that the level of thiamine at which the tissues become "saturated" is about 0.35 mg per 1,000 calories and the excess is excreted in the urine (34, 60, 71). Other studies have also indicated that approximately 0.33 mg thiamine is metabolized daily per 1,000 calories by normal young adult men receiving a diet providing 2,800 calories daily (65, 66). The estimated thiamine requirement of the adult man, based upon urinary thiamine clearance studies, was 0.33 to 0.35 mg per 1,000 calories (75).

Mention should be made with respect to thiamine requirements of the studies in internment camps in South and East Asia during the second world war (81-83). When the thiamine intake was considered in relation to the total calorie intake, it was found that cases of thiamine deficiency were occurring at an estimated level of 0.30 mg per 1,000 calories. It is possible that the nature of the diet fed, physical exertion and the stresses of confinement and associated diseases may have influenced the requirement for thiamine.

Information gathered from nutrition surveys (34) indicates that in

populations where intakes of thiamine fall below 0.40 mg per 1,000 calories (Table 1), such as in Asia and the Far East, thiamine deficiency occurs. Studies on the urinary excretion of thiamine lend support to these findings (Figure 6). Another interesting observation is that the extrapolation

FIGURE 6. – RELATIONSHIP BETWEEN THIAMINE INTAKE AND THIAMINE URINARY EXCRETION IN ADULTS OF 18 COUNTRIES[1]



[1] Data from civilian and military groups surveyed by the Interdepartmental Committee on Nutrition for National Defense of the United States of America (34).

to man of the formulas developed in 1934 (84) for mice, rats, pigeons and dogs indicates that the calculated thiamine requirement for a 70-kilogram man would be 0.30 mg per 1,000 calories, a figure which is in general agreement with values determined experimentally. However, such information provides only a suggestive and not a definite estimation of the thiamine requirement of man.

From the available experimental information, it is evident that a value of approximately 0.33 mg thiamine per 1,000 calories represents the requirement. With an allowance of 20 percent for individual variation (see above), the *recommended intake for thiamine is 0.40 mg per 1,000 calories.*

Adults

Employing the FAO standards for calorie requirements (2), the "reference man," requiring 3,200 calories daily, would need a daily intake of 1.3 mg thiamine (Table 6). Accordingly, the "reference woman," requiring 2,300 calories daily, would need an intake of 0.9 mg thiamine per day. The recommended thiamine intakes per day for adults of different body weights are summarized in Table 9.

Pregnancy

There is little evidence of an increase in thiamine requirement per 1,000 calories in pregnancy (85, 86). Therefore, the recommended intake of 0.40 mg per 1,000 calories is taken to apply to pregnancy (37). Since calorie requirements are believed to increase in pregnancy, the amount of thiamine to be ingested per day would increase.

Lactation

The requirement for thiamine during lactation seems to be adequately met if the extra calorie allowance indicated by FAO (2) is provided, and the figure of 0.40 mg thiamine per 1,000 calories is adhered to (Table 6). This is sufficient to compensate for the thiamine content in the milk (about 0.12 mg per day) (37), as well as for possible additional thiamine utilized in the metabolic process of milk production and secretion.

Infants and children

It is noted that there is a difference between the thiamine/calorie ratio in breast milk (37) from well-nourished mothers (0.20 mg per 1,000 calories) and that in the general recommended intake (0.40 mg per 1,000 calories).

It is agreed that breast feeding is probably the most satisfactory method of meeting the thiamine requirements of the infant under 6 months. It is not known whether the adult recommended intake of 0.40 mg of thiamine per 1,000 calories is applicable to infants older than 6 months. In the absence of more definitive data, however, it is recommended that the thiamine requirement be calculated on this basis.

Similarly, the thiamine requirements for children would be furnished if the calorie requirements for children (2) were satisfied by diets containing 0.40 mg thiamine per 1,000 calories (Table 6).

Factors influencing the requirement

Environmental factors

Composition of the diet

There is some evidence from experimental studies with adults (73) and infants (72) to indicate that the thiamine requirement is related to the dietary ratio of carbohydrates to fat. This concept is supported by animal studies (87, 145). However, in these studies a major increase in the proportion of fat in the diet was found to have a comparatively small effect on thiamine requirements. Thus, it would appear that human diets containing unusually high levels of fat might reduce the requirement for thiamine, and the converse would be true where diets exceedingly high in carbohydrates are encountered. Proteins would fall in an intermediate position between fats and carbohydrates as to their metabolic influence on thiamine requirements, because amino acids may enter the oxidative pathway.

In the case of populations in developing areas, total calorie intake is more closely represented by carbohydrate and protein calories, since diets in those areas are, in general, low in fat. Although this fact may result in

an increase in the thiamine required per 1,000 calories, the significance of this in humans is unknown. From the reported experimental data on animals the effect would appear to be slight.

Climate

Evidence regarding the effect of environmental temperature on the thiamine requirement is conflicting (43, 79). Apparently, cold or hot temperature will have an effect on the absolute requirement of thiamine only to the extent that these climatic changes increase or decrease calorie expenditure. The ratio of thiamine to calories does not appear to change. The losses of thiamine in sweat are not appreciable and would appear to have little influence on the requirements (43).

Other factors

There are suggestions in the literature that altitude may increase the requirement for thiamine but no evidence demonstrating such an effect has been reported for man (43, 79). Adaptation to prolonged intakes of low or high amounts of thiamine may possibly influence the requirement for this vitamin. Current knowledge on this aspect is too meager to warrant further discussion.

Individual factors

Body weight

It is recognized that the thiamine requirement of the human will vary with body weight but it is accepted that this is only to the extent that calorie expenditure is related to body weight (see Chapter 9).

Physical activity

It may be inferred, although there is no direct evidence, that the increase in calorie requirements which accompanies increased physical activity leads to a corresponding increase in the absolute requirement of thiamine with no alteration in the thiamine to calorie ratio. It is recognized that a marked increase in physical activity precipitates symptoms of thiamine deficiency in individuals subsisting on diets inadequate in thiamine. How-

ever, such observations do not indicate any need to modify the recommended thiamine/calorie relationship in situations of heavy physical activity.

Pathological conditions

It is not known whether pathological conditions such as infections, gastrointestinal disease, thyroid disorders, trauma or chronic overconsumption of alcohol modify significantly the requirement for thiamine in relation to calories.

Conclusion

In conclusion, it may be stated that in many of the above instances the resulting modifications in calorie requirements would accordingly result in appropriate thiamine nutriture, provided the recommended thiamine to calorie ratio of intake is maintained. Therefore, no change in the basic recommended intake of 0.40 mg per 1,000 calories is suggested.

Factors influencing content and utilization of thiamine in foods

Thiaminases

Several enzymes capable of destroying thiamine, commonly referred to as thiaminases, have been found to occur in food, e.g., the raw tissues of a number of fish, primarily freshwater fish, and in certain mollusks and crustaceans (146). The enzyme is destroyed by cooking and, consequently, with some exceptions, it may seldom play a significant role in the epidemiology of thiamine deficiency. Heat-stable thiamine-inactivating factors have also been reported to occur in some foods.

Food processing and preparation

Thiamine is relatively stable to heat in the dry form but is otherwise labile to oxidation and is rapidly destroyed in neutral or alkaline solutions. For example, about one third to one half of the thiamine in fruits and vegetables is generally lost during prolonged dehydration. Exposure of

foods to air, to contact with hot water, and to heat as in food preservation or cooking can cause losses in thiamine content. The lime treatment of maize, as practiced in Mexico and Central America, although improving the availability of niacin, causes considerable destruction of the thiamine. Milling of cereals, particularly rice to remove the bran in the production of polished rice, is an important cause of the loss of thiamine in some areas of the world. On the other hand, parboiling of rice enhances the retention of the thiamine. Prolonged storage of foods usually results in a significant loss of thiamine content, the degree of loss depending upon conditions such as pH and temperature. Frozen foods stored at —18°C show little loss of the vitamin for periods of up to one year. The use of sterilization by irradiation for the preservation of foods results in appreciable losses in thiamine content. For the most part, the above-mentioned food losses can be reduced by appropriate techniques of storage and processing or, alternatively, can be compensated for by enrichment of staple food items.

6. RIBOFLAVINE

This vitamin functions as a part of a group of enzymatically active compounds called flavoproteins which contain either flavine mononucleotide or flavine adenine dinucleotide as prosthetic groups, and are involved in the respiratory chain and oxidative phosphorylation. Flavoproteins are relatively unstable, especially when tissue protein is depleted by physiological stresses, dietary deficiency, or disease; under these conditions increased levels of riboflavine are excreted in the urine. At present, no quantitatively important degradation products of riboflavine have been reported and it appears that much of the riboflavine released from a flavoprotein may be reutilized. It is interesting to note from calculations made on the basis of studies on rats, that unlike thiamine, the destruction of riboflavine " through use " cannot be more than 0.025 mg per 1,000 calories per day in man (89), an amount so small as to be negligible. It has been demonstrated frequently (59, 90-93) that the amount of riboflavine in the urine can be lowered to depletion levels in only a few weeks on diets moderately low in riboflavine (0.30 mg per 1,000 calories). The rate of this decrease may be modified if the individual has ingested high levels of riboflavine for long periods (94).

Method of expressing riboflavine requirements

In past years, the requirements for riboflavine because of its relationship to protein metabolism was calculated in terms of protein utilized by the body. More recently, attention has been directed to the relationship of riboflavine to energy expenditure (93). At ordinary levels of intake, where protein and calories are usually closely related, both calculations provide similar amounts per adult and it is only at intakes below 2,000 or above

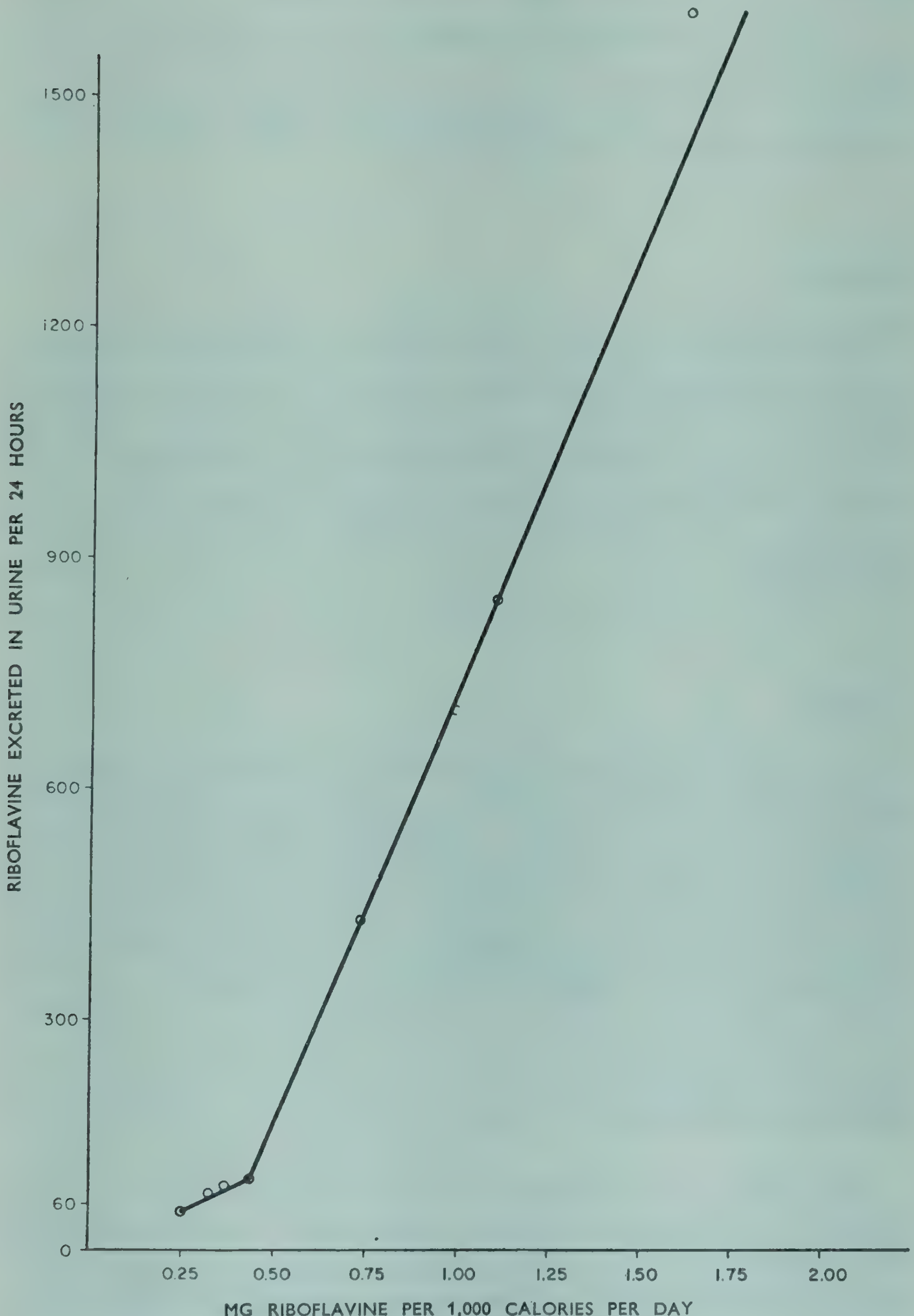
3,000 calories that the results of the two methods of calculation differ significantly. Although riboflavine is involved in both protein and energy metabolism, there are practical advantages in expressing requirements in terms of calories ingested, and this method was chosen.

Principles and methods of estimating requirements

There have been essentially two methods available for estimating human riboflavine requirements: (*a*) population surveys; and (*b*) controlled depletion-repletion studies. In survey studies in which clinical manifestations of ariboflavinosis were related to estimated dietary intake and to levels of riboflavine in the urine, population groups which consumed less than 0.70 mg per adult per day showed a high incidence of clinical deficiency and a significantly low excretion of riboflavine in the urine (less than 40 μg per day) (34). Another recent survey (95) has shown that at a daily intake of 1.00 to 1.30 mg for 2,200 to 2,400 calories, the urinary excretion of riboflavine was over 160 μg, whereas at intakes between 0.50 and 0.80 mg per day the excretion averaged 47 μg. Clinical evidence of deficiency was found only in the latter group.

In depletion-repletion studies, there was incontrovertible clinical evidence of ariboflavinosis in women at intakes of 0.15 mg per 1,000 calories (96) and in men at 0.22 mg (97) and 0.25 mg per 1,000 calories (92). In observations on intakes of 0.31 mg per 1,000 calories (98), of 0.35 mg per 1,000 calories (99) and of 0.36 mg per 1,000 calories (59), there was a marked decrease in riboflavine excretion in many of the subjects to less than 50 μg per day but there were only questionable signs of riboflavine deficiency. In a more recent study, previously supplemented subjects have been on a diet which provided 0.41 mg per 1,000 calories for over two years (94) with no apparent clinical signs of riboflavine deficiency. The urinary excretion of riboflavine in some of these depletion and repletion studies is shown in Figure 7. It illustrates the observation that at levels of ingestion of 0.44 mg per 1,000 calories or higher, there was a significant increase in urinary excretion. These experiments suggest that the body's needs for riboflavine are met at an ingestion level of 0.44 mg per 1,000 calories. This figure was taken as the basis from which the recommended intake was calculated. Adding the variability factor adopted in this report, the group arrived at a *recommended intake for riboflavine of 0.55 mg per 1,000 calories.*

FIGURE 7. – RELATIONSHIP OF URINARY EXCRETION TO LEVEL OF INTAKE OF RIBOFLAVINE AT AN AVERAGE INTAKE OF 2,300 CALORIES [1]



[1] Elgin Studies 94.

Adults

On the basis of the calorie requirements for adults (2), the recommended intake of 0.55 mg per 1,000 calories would provide 1.80 mg for the "reference man" (3,200 calories). The "reference woman" (2,300 calories) would need an intake of 1.30 mg per day.

Pregnancy

Although there have been some studies to indicate that late in pregnancy women excrete less riboflavine than do nonpregnant women on the same intake (100-102), in the absence of more definite data it was decided not to recommend any additional increase in riboflavine over that supplied by the increase in calories allowed during pregnancy (2). Accordingly, the recommended intake for pregnancy remains at 0.55 mg per 1,000 calories.

Lactation

The average daily breast milk output and its riboflavine content have been computed as 850 ml and 0.32 mg, respectively (37). The extra calorie allowance of 1,000 calories recommended during lactation would be expected to supplement the riboflavine intake by 0.55 mg per day. It is believed that this amount is not only sufficient to cover the riboflavine secreted in the milk but also provides a reasonable allowance for the possible utilization of the vitamin in the production of milk.

Infants and children

For infants of 0 to 6 months of age, the evidence indicates that breast feeding by a well-nourished mother supplies sufficient riboflavine to meet the requirement. It is not known whether the recommended intake of 0.55 mg riboflavine per 1,000 calories is applicable to older infants. However, in the absence of more definitive data, it was decided to use

this ratio. On the same basis, a riboflavine intake of 0.55 mg per 1,000 calories is considered satisfactory for children. The recommended levels for the different age groups are indicated in Table 6.

Factors affecting requirements for riboflavine

Environmental

Composition of diet

Although the results of animal experiments have suggested that excess carbohydrate reduces the riboflavine requirement and, conversely, excess fat increases the needs for the vitamin, there are no comparable data for man showing the effects of altering the ratio of carbohydrate to fat on the riboflavine requirement (103). Neither is there evidence, in areas of the world where the fat intake in the diet is high, that clinical manifestations of riboflavine deficiency occur more frequently than would be expected on the basis of riboflavine intake. It is suggested, therefore, that the recommended intake of 0.55 mg per 1,000 calories will not be affected to any practical degree by a change in the carbohydrate to fat ratio in human dietaries.

The close relationship between riboflavine and protein metabolism has been discussed earlier. Under conditions of calorie balance and adequacy of dietary protein there is no evidence to suggest that any alteration has to be made in the recommended intake of riboflavine for variation in protein intake. It should be noted that a prolonged state of negative nitrogen balance in the individual results in a significant loss of riboflavine in the urine (93, 147). The relationship between riboflavine on the one hand and thiamine and ascorbic acid nutrition on the other has been recognized from animal experiments (148, 149). It has been shown in rats that in thiamine deficiency there is a pronounced disturbance in riboflavine metabolism mainly because of its poor absorption; in riboflavine deficiency there is no apparent disturbance of thiamine metabolism (104). There are no similar data for humans.

Climate

The influence of climate on riboflavine requirements has been studied (43). The results do not indicate an increased need over the recommended intake (0.55 mg per 1,000 calories) stated for adults.

Individual factors

Body weight

The riboflavine requirement is probably related to body size. However, in view of the fact that the recommended intake of riboflavine is expressed in terms of calories, and as calorie requirements are already adjusted to body size, there is no need to make a separate adjustment for riboflavine in this respect.

The arguments advanced for thiamine need (see page 36) are also applicable to riboflavine requirements in relation to physical activity.

Pathological factors

There is no clear evidence in man to establish an effect of infections on riboflavine requirements (105).

Factors influencing availability of riboflavine in foods

Riboflavine is widely distributed in plant and animal foods. Among the good sources of riboflavine are milk, eggs, fish, kidney, liver, heart, muscle and growing leafy vegetables. Cereals and legumes are not rich sources of the vitamin, but due to the large quantities consumed, they supply much of the riboflavine in human diets. Milling of grains deprives the flour of much of the vitamin because the major part of the vitamin is in the germ and bran. However, germination increases the riboflavine content of cereals or pulses.

Ordinary processes of cooking do not destroy appreciable quantities of riboflavine, but cooking in an alkaline medium will accelerate the rate of destruction. Processing of foods such as canning, slow freezing and thawing and dehydration also cause losses of riboflavine. The technique of sun-drying as practiced in tropical countries for fish, vegetables and other food products will cause considerable destruction of riboflavine.

7. NIACIN

Niacin is incorporated into nicotinamide adenine dinucleotides to form the prosthetic group of certain enzymes that take part in electron transfer reactions in the respiratory chain and in oxidative phosphorylation. There are several metabolic products of niacin of which N^1-methylnicotinamide and its pyridones are most important to the study of niacin metabolism. Since the discovery of the conversion in the rat of tryptophan to niacin (106) any consideration of niacin metabolism must include this potential source of niacin. It is not known how much the conversion of tryptophan to niacin is affected when tryptophan is the limiting factor in the diet. In addition, the food source of niacin in mixed diets should be evaluated since niacin may exist in bound forms (e.g., niacytin) in cereals but not in pulses and foods of animal origin (107).

Principles and methods of estimating requirements

Intakes of less than 7.50 mg niacin per day have been associated with the occurrence of pellagra (108-111) but these studies were made before the contribution of tryptophan to the formation of niacin in human nutrition was fully acknowledged. Tryptophan had been used to ameliorate symptoms of pellagra (112-114) but quantitative evaluation of the contribution of tryptophan to niacin nutriture in man had to await further experimentation. To define its contribution the term "niacin equivalent" was introduced (115). This term permitted the calculation of the combined effects of both niacin and tryptophan. Thus, on the basis of the levels of N^1-methylnicotinamide excretion in the urine of experimental subjects (116-118) on a variety of diets, it has been estimated that, in humans, approximately 60 mg tryptophan give rise to 1 mg niacin, a relationship not unlike the 50 to 1 ratio noted in baby pigs (119). There

is some evidence that pregnant women can convert tryptophan to niacin (118, 120) more efficiently than other adults. From such considerations the *group adopted the definition that one niacin equivalent is equal to either 1 mg niacin or 60 mg tryptophan.* Table 4 shows the niacin equivalents of foods like milk and eggs, which provide very little preformed niacin but are not pellagragenic.

TABLE 4. – NIACIN EQUIVALENTS IN REPRESENTATIVE FOODS[1]

Food	Niacin	Tryptophan	Niacin equivalents
	mg/1,000 calories		per 1,000 calories
Cow's milk	1.2	673	12.4
Human milk	2.5	443	9.9
Beef, round	24.7	1 280	46.0
Whole eggs	0.6	1 150	19.8
Salt pork	1.2	61	2.2
Wheat flour, white	2.5	297	7.4
Corn grits	1.8	70	3.0
Corn	5.0	106	6.7

[1] Reproduced from Horwitt, M. K. *et al.* (121).

Estimation of requirements

When the intake of niacin equivalents by subjects on experimental diets (121) is compared to the incidence of clinical lesions (Table 5), it can be seen that 4.4 niacin equivalents per 1,000 calories approximates to the minimum requirement for the prevention of clinical deficiency in adult subjects. Leaving any corrections for bound niacin in the diet for later consideration, the relationship between the excretion of niacin derivatives and the level of niacin equivalents consumed may be estimated from the following:

In a depletion-repletion study (97) in which the basal diet provided 4.4 niacin equivalents per 1,000 calories, supplements of 50 mg tryptophan or 10 g lactalbumin or 30 g lactalbumin or 10 mg niacin, respectively, were incorporated into isocaloric diets which provided 2,300 calories.

TABLE 5. – RELATIONSHIP BETWEEN NIACIN INTAKE AND CLINICAL SYMPTOMS IN CONTROLLED EXPERIMENTS[1]

Diet	Calories	Niacin[2] (mg)	Tryptophan (mg)	Niacin equivalents	Niacin equivalents per 1 000 calories[3]	Proportion of subjects with pellagra symptoms
Tulane "corn"[4] .	1 700–2 100	4.4–5.4	170–207	7.3–8.7	(3.7–4.4)	[5]10/10
Tulane "wheat"[4] .	1 600–1 900	4.2–5.0	177–200	7.3–8.3	(3.7–4.2)	3/5
Goldberger[6] . . .	3 000	6.7	330	12.2	4.1	6/11
Elgin	2 070	5.2	238	9.2	4.4	0/1
Elgin	2 300	5.8	265	10.2	4.4	0/11
Elgin	2 530	6.4	292	11.3	4.4	0/1
Elgin	2 760	7.0	318	12.3	4.4	0/2
Tulane "corn"[7] + niacin	1 970	6.7	190	9.9	4.9	0/1

[1] Reproduced from Horwitt, M. K. *et al.* (121). — [2] Includes bound niacin. — [3] Diets providing less than 2,000 calories are arbitrarily calculated as containing 2,000 calories. — [4] Calculated from Goldsmith *et al.* (117). — [5] Three of these subjects, two of whom consumed the most niacin equivalents, 8.7, were considered to have "mild niacin deficiency." The other seven, who consumed from 7.3 to 8.6 niacin equivalents, had "severe niacin deficiency." — [6] Calculated from Frazier and Friedemann (110). — [7] Same as "Tulane corn" above plus 2 mg niacinamide per day.

In the group receiving 10 g lactalbumin, which added 2.5 niacin equivalents, the excretion of N[1]-methylnicotinamide increased to levels above those noted in deficiency states for about half the subjects. When 30 g lactalbumin, representing 7.5 niacin equivalents, were added to the protein in the diet, there was a marked increase in niacin metabolites in the urine indicating a niacin tissue saturation in all the subjects. The other diets produced even higher levels of excretion. The basal diet, plus 10 g or 30 g lactalbumin, provided a total of 5.5 or 7.7 niacin equivalents per 1,000 calories, respectively. Therefore, it was accepted that 5.5 niacin equivalents per 1,000 calories per day, an intake at which no clinical signs were observed and at which some of the subjects showed an increase in urinary excretion of niacin metabolites, is the figure to be taken as the level from which the recommended intake is calculated. The addition of the factor to account for individual variation gives a *recommended intake of 6.6 niacin equivalents per 1,000 calories per day.*

To calculate niacin equivalents in a diet, the expert group has accepted the ratio 60 mg of tryptophan as equivalent to 1 mg niacin for all

physiological states. The group recognized that this relationship may not hold under conditions where tryptophan forms the limiting amino acid in the diet.

Adults

On the basis of calorie requirements for adults (2), the recommended intake of 6.6 niacin equivalents per 1,000 calories per day would provide 21.1 niacin equivalents for the "reference man" (3,200 calories) and 15.2 niacin equivalents for the "reference woman" (2,300 calories).

Pregnancy and lactation

The same considerations put forward for riboflavine and thiamine apply to niacin. There is no evidence that the requirement for niacin equivalents is increased in pregnancy and lactation above that satisfied by the recommended intake of 6.6 niacin equivalents per 1,000 calories per day.

Infants and children

The same considerations as for riboflavine and thiamine apply to niacin. The recommended intake of 6.6 niacin equivalents per 1,000 calories per day is accepted for children of 6 months or older (see Table 6). For infants 0 to 6 months, it is accepted that breast feeding by well-nourished mothers will supply adequate niacin equivalents to fulfill the needs for this age group.

Factors affecting requirements for niacin

Environmental

Composition of the diet

The fact that pellagra is a disease most often found in people who consume maize, which is deficient in tryptophan and in which the niacin may not be available to the body, is discussed on page 5. In areas of the world where maize is treated with lime there is a low incidence of pellagra.

Research with animals (122) has indicated the possibility that certain amino acid imbalances may increase the requirement for niacin or may interfere in its formation from tryptophan. Similarly, when the tryptophan intake is limiting, the usual conversion to niacin may not occur. Whether or not such effects may be of importance in human nutrition is not known. No definite effect of the proportion of carbohydrate or fat on niacin requirements has been established.

Climate

Although the cutaneous changes of pellagra are nearly always more easily demonstrated in areas of the skin exposed to sunlight, climate *per se* has not been associated with changes in the requirement for niacin.

INDIVIDUAL FACTORS

Body weight

Although it is recognized that a larger person will have a larger niacin requirement, such an increase is considered to be more a function of calorie requirements than of any other physiological parameter. Accordingly, no adjustment is made for body weight since increased calorie needs automatically increase the recommended intake of niacin.

Physical activity

It has been noted that pellagra is more frequently observed among agricultural workers. While this may be associated with an increased calorie intake without a proportional increase in niacin intake (depending on the additional food eaten), it seems probable that this association is due to the aggravation of dermal lesions by exposure to sunlight. No adjustment in the basic recommended intake (6.6 niacin equivalents per 1,000 calories) is suggested for physical activity.

Factors affecting availability of niacin in foods

The bound form of the vitamin, termed "niacytin," which apparently represents a major proportion of the niacin in cereals, is the most important factor affecting the availability of niacin from foods (107). Another bound form of nicotinic acid has been described as occurring in wheat and

rice bran (123). Niacytin, which appears to be a niacin ester of a complicated configuration (124), is not available to pigs, rats, poultry and bacteria as a source of niacin (107). There is suggestive evidence that niacytin may also be unavailable to man.

Some tentative confirmation of the unavailability to man of the niacin in maize may be noted in Table 4, in which maize is shown to have a higher niacin equivalent per 1,000 calories from niacin alone (5.0 niacin equivalents) than the level found to produce symptoms of pellagra ($<$4.4 niacin equivalents) shown in Table 5.

Lime treatment of maize as used in Mexico and in Central America for the preparation of tortilla releases niacin from its bound form and makes it fully available to the rat (125). This may explain in part the low incidence of pellagra in populations consuming this food. In addition, however, certain other food sources rich in available niacin may contribute significantly to the pellagra-preventive effect of the diet. Thus, pulses, some beverages such as pulque and kaffir beer and coffee are important sources of niacin (107).

Of the vitamins, niacin is unique in that it is exceedingly stable not only in the dry state but also in solution. In foods, it can withstand reasonable periods of heating or autoclaving without destruction. It is also fairly stable in acid or alkaline media. The usual methods of food preservation or storage for prolonged periods have little effect. The vitamin is, however, subject to some leaching losses during the preparation of foods depending upon cooking practices. Usually, these losses will not exceed 15 to 20 percent. Tryptophan is also very stable to the usual treatments encountered in food processing, storage and cooking.

8. SUMMARY OF RECOMMENDED INTAKES OF THIAMINE, RIBOFLAVINE AND NIACIN

Table 6 summarizes the daily recommended intakes of thiamine, riboflavine and niacin for various ages. These figures are based upon the recommended intakes described in the earlier chapters and the calorie intakes recommended by the FAO Second Committee on Calorie Requirements (2).

TABLE 6. – DAILY RECOMMENDED INTAKES OF THIAMINE, RIBOFLAVINE AND NIACIN

Age	Calories/day	Thiamine (mg)	Riboflavine (mg)	Niacin[1] equivalents
0-3 months[2]	120/kg	—	—	—
4-6 " [2]	110/kg	—	—	—
7-12 "	1 000	0.4	0.6	6.6
1 year	1 150	0.5	0.6	7.6
2 years	1 300	0.5	0.7	8.6
3 "	1 450	0.6	0.8	9.6
4-6 years	1 700	0.7	0.9	11.2
7-9 "	2 100	0.8	1.2	13.9
10-12 "	2 500	1.0	1.4	16.5
13-15 (boys)	3 100	1.2	1.7	20.4
(girls)	2 600	1.0	1.4	17.2
16-19 (boys)	3 600	1.4	2.0	23.8
(girls)	2 400	1.0	1.3	15.8
Adults[3] (man)	3 200	1.3	1.8	21.1
(woman)	2 300	0.9	1.3	15.2

[1] A niacin equivalent is 1 mg niacin or 60 mg L-tryptophan. — [2] For children 0 to 6 months it is accepted that breast feeding by a well-nourished mother is the best way to satisfy the nutritional requirements for thiamine, riboflavine and niacin. — [3] For recommended intakes of thiamine, riboflavine and niacin for adults of different body weights, see Table 9.

9. PRACTICAL APPLICATIONS

As stated in Chapter 2, the main purposes of the recommended intakes for vitamin A, thiamine, riboflavine and niacin are to evaluate the intakes of population groups, to plan diets and food supplies and to serve as a guide for public health nutrition programs. The present chapter is concerned with the application of the recommendations for the above purposes.

Vitamin A

The recommended intakes of retinol for adults of both sexes, for pregnancy and lactation, for children and adolescents, are given in Chapter 3 (Table 3). As explained in that chapter, it was not deemed necessary to make additional provision for individual variation nor to make adjustments for small differences in body weight between individuals within the same age group, since the margin between the amount necessary to prevent clinical signs of deficiency and the recommended intake is sufficiently large. Furthermore, available information indicates that factors such as physical activity, climate, etc., do not influence requirements for retinol.

Modification of recommended intake for diets containing carotenes

Reference has already been made (page 23) to the fact that human diets contain both retinol and carotenes in widely varying proportions. The major source of vitamin A in most diets is β-carotene, which is not utilized in the human body as efficiently as retinol. In the human, 1 μg β-carotene in the diet is taken to have the same biological activity as only 0.167 μg retinol. The adjustment of the recommended intake of reti-

nol in accordance with the biological activity of vitamin A compounds in the diet can be made by the formula given on page 25. The application of this formula to diets with 40 to 100 percent carotene is shown in Table 7.

Vitamin A values in food composition tables

The formula requires data on dietary intakes of retinol and β-carotene and, consequently, it is now essential that tables of food composition report separately the amount of these two nutrients in foods.

A first approximation of the retinol and β-carotene content of foods may be made by assuming that animal-source foods contain only retinol and vegetable foods contain only β-carotene.

Vitamin A values in practically all of the existing tables are generally given in IU of vitamin A activity. The IU values can be converted to micrograms by applying the following factors:

1 IU of vitamin A = 0.3 μg retinol
= 0.6 μg β-carotene
= 1.2 μg other total mixed carotenoids with vitamin A activity

Some data are now available on the estimated distribution of vitamin A activity in various foods (Appendix 6). A few examples are given in Appendix 5 for the calculation of the retinol and carotenoid contents of foods.

In order to avoid confusion, it may be noted here that the application of the above-mentioned factors will yield values of these nutrients as they occur in foods. In arriving at the recommended intakes, the factor of utilization efficiency has to be taken into account, as discussed on page 25.

Reporting dietary survey data

When dietary surveys report intakes of both retinol and β-carotene separately, the practice of reporting total "vitamin A" intake in IU can be discontinued

National food balance sheets can also provide information necessary for estimating the proportion of carotene in the food supplies of a particular country. However, the limitations of this information must be recognized, since statistical data in many countries are still inadequate and inaccurate, and statistics on the main sources of vitamin A such as green leafy and yellow vegetables are not always available.

TABLE 7. – RECOMMENDED INTAKES OF VITAMIN A (μg) AT VARIOUS AGES IN RELATION TO THE PROPORTION OF β-CAROTENE IN THE DIET[1]

Age	Percentage of β-carotene in diet											
	0	40	50	60	65	70	75	80	85	90	95	100
0-6 months	—	—	—	—	—	—	—	—	—	—	—	—
7-12 "	300	450	525	600	650	725	800	900	1 025	1 200	1 450	1 800
1 year, 2 years, 3 "	250	375	425	500	550	600	675	750	850	1 000	1 200	1 500
4-6 "	300	450	525	600	650	725	800	900	1 025	1 200	1 450	1 800
7-9 "	400	600	675	800	875	950	1 075	1 200	1 375	1 600	1 925	2 400
10-12 "	575	850	975	1 150	1 250	1 375	1 530	1 725	1 975	2 300	2 750	3 450
13-15 "	725	1 100	1 250	1 450	1 575	1 750	1 950	2 175	2 500	2 900	3 450	4 250
16-19 "	750	1 125	1 275	1 500	1 650	1 800	2 000	2 250	2 575	3 000	3 600	4 500
Adults	750	1 125	1 275	1 500	1 650	1 800	2 000	2 250	2 575	3 000	3 600	4 500

[1] Expressed as $\frac{\beta\text{-carotene}}{\beta\text{-carotene} + \text{retinol}}$ (μg). Other vitamin A-active carotenoids are expressed in terms of β-carotene, on the basis that 2 μg other vitamin A-active carotenoids = 1 μg β-carotene; retinyl esters expressed in terms of their retinol content.

ESTIMATION OF RECOMMENDED INTAKES OF POPULATION GROUPS

Data on the age and sex distribution of the population and the proportion of pregnant and lactating women are required for estimating the recommended intakes of a population. In this case, the number of pregnant women is not important since no additional intake has been recommended for pregnancy. Similarly, it will not be necessary to calculate the number of lactating women if the number of infants is known. It may be recalled that during the first six months of life, the allowance (to the infant or additional allowance to the mother) is about 450 μg retinol per day. An example of the calculated weighted average recommended intake per caput per day for a population is given in Table 8.

TABLE 8. — ESTIMATION OF RECOMMENDED INTAKES OF VITAMIN A-ACTIVE COMPOUNDS[1]

Age	Population	Recommended intake, μg/person/day		Total recommended intake μg/day	
		Retinol	Vitamin A-active compounds	Retinol	Vitamin A-active compounds
	Thousand				
0-6 months	54	[2]450	1 194	24 300	64 476
7-12 "	54	300	800	16 200	43 200
1-3 years	231	250	675	57 750	155 925
4-6 "	200.2	300	800	60 060	160 160
7-9 "	184	400	1 075	73 600	197 800
10-12 "	160.8	575	1 530	92 460	246 024
13-15 " (boys)	83.5	725	1 950	60 538	162 825
13-15 " (girls)	84.6	725	1 950	61 335	164 970
16-19 " (boys)	113.6	750	2 000	85 200	227 200
16-19 " (girls)	132	750	2 000	99 000	264 000
Adults (man)	670	750	2 000	502 500	1 340 000
Adults (woman)	705	750	2 000	528 750	1 410 000
Total	2 672.7			1 661 693	4 436 580

RECOMMENDED INTAKE for Retinol = 622 μg/caput/day[3]
Vitamin A-active compounds = 1 660 μg/caput/day[3]

[1] The calculations apply to a country where the proportion of carotene in the national diet is generally 75 percent. — [2] This figure represents the additional requirement for lactation. There is no additional requirement for pregnancy. — [3] Rounded to the nearest whole number nending in 0 or 5.

Assessing vitamin A adequacy of diets and food supplies

The comparison of the actual or estimated intake of vitamin A as observed from food consumption surveys with the recommended intake will provide a measure of the adequacy of the diet. Since the estimated intake will be reported both as retinol and carotene, for purposes of comparison it will be necessary to convert the carotene to retinol and add this value to the retinol intake to arrive at the total retinol equivalent of the estimated intake. This total can then be compared directly with the recommended intake for retinol of the individual or population group concerned. For example, if an adult has been found to be consuming 250 μg of retinol and 2,400 μg β-carotene, this would be equivalent to a total retinol intake of $250 + \frac{2\,400}{6} = 650$ μg. This can be compared to the recommended intake of 750 μg of retinol for an adult. *However, in reporting the actual dietary intakes it is still important to give both the retinol and β-carotene intakes rather than just the equivalent retinol intakes, since the suggested correction for the efficiency of utilization of β-carotene is still tentative.* The intake of retinyl esters and of carotenoids other than β-carotene should be converted to retinol and β-carotene, as explained earlier.

In appraising the vitamin A adequacy of the food supply it will also be necessary to determine its content of retinol and carotene. As a first approximation, in the absence of food composition tables giving the retinol and carotene value of foods, the approach suggested on page 53, whereby vegetable and animal foods are assumed to contain carotene and retinol respectively, can be followed. Once the carotene and retinol content of the food supply is determined, the above procedure of determining the equivalent retinol content and comparing it with the recommended intake will determine the adequacy of the food supply with regard to vitamin A. In interpreting the findings, the limitations of food balance sheet data, pointed out above (see page 53), should be borne in mind.

Meeting the recommended intake for vitamin A

Table 7 illustrates the considerable increase in the recommended intakes of vitamin A with an increase in the proportion of carotene in the diet. It also demonstrates the difficulty which arises when vitamin A requirements must be met from foods of vegetable origin alone.

This emphasizes the need for developing animal resources and considering side by side the means for improving diets in protein and vitamin A. For example, the dairy industry can solve both problems, provided cow's milk is not deprived of its vitamin A by skimming off the fat. Unfortunately, milk production in most developing countries remains small due to numerous difficulties such as climate, disease, feed shortage, etc. Since all these require a long time to overcome, imported milk products may have to play an important role for some time initially. The fortification of skim milk products with vitamin A should be encouraged further.

Eggs are an excellent source of retinol and may prove to be a practical method of supplementing vegetable diets, since the efficiency of poultry production has increased in many countries, resulting in a substantial reduction in the price of eggs.

Red palm oil, which is a very rich source of β-carotene (240 to 480 μg/g) is extensively produced in West and Central Africa and parts of the Far East, and its cultivation is beginning to spread to other tropical areas. Apart from its medicinal use, its culinary use in admixture with other edible vegetable oils deserves to be encouraged.

Green leafy vegetables, such as the young leaves of *Ipomoea* (sweet potato and swamp cabbage), cassava, amaranth, horseradish, etc., are rich sources of carotenes. The yellow vegetables and fruits such as carrots, mangoes and papayas are also good sources. They are common foods in developing countries but considerable increases in their production and consumption are most desirable. The yields of these fruits and vegetables can be increased relatively cheaply through scientific production techniques.

Fresh immature legumes (green string beans, lima beans, peas, etc.) before they reach the mature dried stage (grain legumes) are also good sources of both protein and carotenes. Much can be done to improve their availability through improved cultivation techniques.

A program of general nutrition education is important as people's food habits need to be influenced toward consumption of sufficient quantities of cheap sources of vitamin A. There should be special emphasis on the incorporation of green leafy and yellow vegetables and fruits and of eggs into the diet, along with increasing the consumption of inexpensive protein-rich foods such as grain legumes.

Apart from the long-term measures, immediate ones should be considered and an important one among the latter is the provision of

supplements in the form of special foods or nutrient preparations under appropriate supervision of the health services.

In areas where protein-calorie malnutrition is known to exist, it is important to recognize that this deficiency may have a detrimental effect upon the utilization of carotene. Hence, attention should be directed to the improvement of both protein and vitamin A intake. In such areas, particularly when significant improvement of protein intake is difficult, attention might preferably be directed to sources of retinol.

Special considerations

Vitamin A deficiency is an important problem in infants and young children in many areas of the world. As was suggested in Chapter 1, this may be attributed in part to a failure to build up significant liver stores of vitamin A in early infancy; in these areas, the vitamin A content of breast milk may be very low (see Table 2). As an immediate program to deal with the problem of childhood vitamin A deficiency, special attention might be directed to the provision of vitamin A during pregnancy and lactation with the object of ensuring an adequate level of vitamin A in breast milk and thus of the vitamin A stores in the livers of young infants.

From the considerations presented in Chapter 3 it can be estimated that the total vitamin A cost of pregnancy and six months of lactation is approximately 81,000 μg retinol over and above the normal adult requirement. Nearly all of this additional requirement is for lactation. However, since vitamin A is stored in the liver, it may be possible to anticipate the heavy needs of lactation by supplying additional vitamin A during pregnancy. Preliminary studies have suggested that large supplements of retinol during pregnancy are effective in improving the vitamin A content of breast milk. Preparations containing β-carotene, such as red palm oil, may also be effective. Further research is needed to establish the suitable dosage schedules. These considerations would apply only to populations in which breast feeding is practiced and in which the dietary supply of vitamin A is likely to be inadequate during lactation.

As a further, or alternate, measure to reduce the incidence of vitamin A deficiency in certain areas, consideration might be given to the provision of periodic doses of vitamin A to infants and children in order to supplement an inadequate dietary intake. The size of the periodic dose would vary with the interval between doses and the dietary supply. Again it is

to be recalled that in areas where protein-calorie malnutrition is prevalent, the utilization of β-carotene may be impaired and retinol would be the preferred source of vitamin A.

Effect of infections

The occurrence of hypovitaminosis A in a large number of developing countries, particularly in South and East Asia, was described in Chapter 1. Vitamin A or multiple vitamin deficiency syndromes are commonly associated with protein-calorie deficiencies in infants and young children and in many areas of the world form the prevailing pattern of malnutrition. It is also well known that, in these same areas, populations are subjected to hazards of infection which are much reduced in developed countries. The WHO Expert Committee on Nutrition and Infection (105) which recently examined the interaction between malnutrition and infection has emphasized the synergistic effect of these two conditions. It would appear from the report of this committee that one of the ways to combat the severity of the effect of infections is to ensure adequate nutrition of the population, particularly that of the vulnerable groups. Furthermore, there is evidence to show that infection may increase the requirement in more ways than one. Hence, it is all the more important that in such situations all efforts be made to ensure adequate nutrition of such populations with regard to essential nutrients.

Hypovitaminosis A in young children is nearly always accompanied by infectious diseases, especially affecting the gastrointestinal and respiratory tracts. Infection may precipitate clinical manifestations of vitamin deficiency and, on the other hand, the pre-existing deficiency state may influence the severity and outcome of illness caused by infection. Where the majority of children are already in a state of moderate to severe protein-calorie deficiency, it is easy to understand why the associated vitamin A deficiency greatly diminishes the chances of survival of the child suffering from protein-calorie deficiency. Xerophthalmia as a complication of protein malnutrition varies from between 1 and 2 percent (e.g., Lebanon, Uganda) to as high as 75 percent (e.g., Indonesia). Such differences may be partly explained on the basis of the vitamin A value of the staple food (steamed plantain in Uganda and rice in Indonesia).

The marked seasonal variations noted in many areas in the occurrence of xerophthalmia can be explained partly by this intimate relationship of vitamin A deficiency to infection (7) and partly by the seasonal availa-

bility of green and yellow vegetables, and fruits. Gastroenteritis of infants ("summer diarrhea"), so common in partially breast-fed or inadequately bottle-fed babies in the subtropical regions, frequently gives rise to xerophthalmia in the late summer and autumn months. Depletion is often enhanced by "therapeutic" diets of semistarvation, either traditional or even instituted on the advice of the physician. Measles, by its serious complications, including involvement of the cornea, among inadequately fed infants and children often precipitates xerophthalmia during the winter months.

Chronic infections, such as tuberculosis and malaria, cause a gradual depletion of liver stores of vitamin A. In the rare instances of xerophthalmia occurring in older children or adults, a history of hepatitis leading to cirrhosis is frequently found. Night blindness during pregnancy and keratomalacia commencing a few weeks after delivery also account for a proportion of the sporadically arising cases in adult life.

Thiamine, riboflavine and niacin

The recommended intakes for thiamine, riboflavine and niacin are summarized in Table 6. As stated previously (Chapter 4), requirements for these nutrients are related to energy expenditure and, therefore, the recommended intakes are presented in terms of mg per 1,000 calories. It is pertinent to recall that the individual should be in calorie balance because it is only under this condition that energy expenditure and calorie intake are equal.

The calculation of calorie requirements is described in the FAO publication *Calorie requirements*, Report of the Second Committee on Calorie Requirements, FAO Nutritional Studies No. 15, 1957 (2). This method includes adjustments for body weight, age and environmental temperature.

Recommended intakes for various age groups

The recommended intakes for adults are based on the "reference man" and "reference woman" as described in the report on calorie requirements (2). It will be necessary to adjust for body weight, age and environmental temperature when adults differ from the reference man and woman in all of these respects. The recommended intakes when adjusted for body weight are shown in Table 9.

TABLE 9. – RECOMMENDED INTAKES FOR ADULTS OF DIFFERENT BODY WEIGHTS[1]

MEN

Recommended intake	Body weight							
	Kilograms							
	45	50	55	60	65	70	75	80
Thiamine, mg/day . . .	1.0	1.1	1.1	1.2	1.3	1.4	1.4	1.5
Riboflavine " " . . .	1.3	1.5	1.6	1.7	1.8	1.9	2.0	2.1
Niacin equivalents[2] . .	16.3	17.5	18.7	19.9	21.1	22.3	23.5	24.6

WOMEN

Recommended intake	Body weight							
	Kilograms							
	35	40	45	50	55	60	65	70
Thiamine, mg/day . . .	0.7	0.7	0.8	0.9	0.9	1.0	1.0	1.1
Riboflavine " " . . .	0.9	1.0	1.1	1.2	1.3	1.4	1.4	1.5
Niacin equivalents[2] . .	11.0	12.1	13.2	14.2	15.2	16.2	17.2	18.2

[1] Calorie needs of adults according to body weight taken from page 36 of the FAO report, *Calorie requirements*, 1957 (2). — [2] Includes preformed niacin and that derived from tryptophan; 60 mg tryptophan = 1 mg niacin.

However, since the calorie requirements are adjusted for these factors and the recommended intakes are expressed per 1,000 calories, all that remains to be done is to multiply these by the calorie requirements. This same procedure is applicable to children, adolescents and pregnant and nursing women.

RECOMMENDED INTAKES OF POPULATIONS

The "actual requirement scale" for calories (2, page 43) would be the basis for calculating the recommended intakes, using 0.40 and 0.55 mg per 1,000 calories for thiamine and riboflavine, respectively, and 6.6 niacin equivalents per 1,000 calories.

Evaluation of adequacy of dietaries or food supplies

From food balance sheet data the intakes of thiamine, riboflavine and niacin may be calculated per 1,000 calories and compared with the recommended intakes of 0.40 mg thiamine, 0.55 mg riboflavine and 6.6 niacin equivalents per 1,000 calories. For purposes of evaluating national food supplies, it is not necessary to calculate the per caput intakes of these vitamins.

In the case of niacin, since the recommended intakes are expressed in terms of "niacin equivalents," it is necessary that data on food consumption include an estimation of tryptophan intake. Food composition tables should itemize the niacin equivalent content of foods or provide data for both preformed niacin and tryptophan.

Ensuring adequate intakes of thiamine, riboflavine and niacin

The low levels of intake in developing areas for these vitamins, particularly thiamine and riboflavine, and the consequent occurrence of vitamin deficiencies either as severe disease or in a chronic mild form were described in Chapter 1.

Important sources of the three vitamins are various kinds of pulses, meat, fish, milk and eggs which are also rich in protein. Hence, some methods suggested for the improvement of protein and vitamin A intakes, such as addition to the diet of milk and other foods of animal origin and some legumes or pulses or well-prepared protein-rich food mixtures from good quality vegetable sources, are also applicable to thiamine, riboflavine and niacin.

The consumption of polished milled rice has been closely associated with the prevalence of beriberi in many areas. Home-pounded or parboiled rice could be encouraged but many cultural and social problems are involved in this approach. For the same reason, the consumption of some foods which are a rich source of thiamine, such as pork, can be encouraged only when the dietary item is acceptable to the population concerned.

The infrequency of pellagra among maize eaters in Latin America and in Indonesia has been attributed to the nutritional merits of some of the numerous varieties of beans which are good sources of preformed niacin and tryptophan and to lime treatment of maize in Central America. Such practices might be examined for possible introduction in other maize-eating populations.

Measures to increase the production of these important foods will, of course, require a vigorous program in nutrition education, not only to encourage consumption of the foods but also to improve dietary practices and food habits. Emphasis should be placed not only on encouraging greater production and consumption of the foods rich in these nutrients but also on proper preparation and cooking methods for these foods, as well as the staples (such as rice and maize), to conserve their nutritive value.

Finally, the recommended intakes in this report provide an appropriate basis for the establishment of a policy of food enrichment with vitamins. In some areas of the world, this procedure is already employed in order to restore to the original level certain B vitamins lost from cereals through processing, or to add vitamins A and D to skim milk. Such measures are of great importance in those areas where the consumption of highly processed foods cannot be supplemented with other fresh sources of these vitamins.

Special needs of vulnerable groups

As an immediate measure, it may be necessary to consider the provision of vitamin supplements to lactating women and young children. This should be given particular consideration in areas where infantile beriberi is known to occur. It has been demonstrated that this is often attributable to a very low thiamine content in breast milk and that the mothers of these children often show symptoms of thiamine deficiency. Thiamine supplements given to such mothers to restore milk thiamine levels to normal, or given to the infants, would prevent beriberi. Unlike vitamin A, it is not probable that large supplements of the B vitamins during pregnancy would be stored to provide the needs of lactation.

In large part, reliance will have to be placed on educating mothers in infant- and child-feeding practices to ensure an adequate intake of thiamine, riboflavine and niacin in these age groups. Here the problem is similar to that encountered in protein-calorie malnutrition. Attempts to introduce relatively cheap, locally available and appropriately processed protein-rich foods for the feeding of infants and young children will also contribute to the objective of improving the intake of thiamine, riboflavine and niacin, if the content of these nutrients is given consideration in developing such foods.

10. SUGGESTIONS FOR FURTHER RESEARCH

General problems

During its discussions, the group recognized gaps in existing knowledge and agreed on the need for further research on the following points:

Levels of vitamin intake and nutritional status

More information is needed about the long-term effects of various levels of vitamin intake on nutritional status. It is necessary to investigate whether, and to what extent, the body can adapt itself to different levels of vitamin intake without deleterious effects. For this purpose, it is necessary to carry out studies on population groups habitually consuming high or low levels of vitamins, particularly with a view to relating clinical symptoms of deficiency or excess to the dietary intakes of the vitamins. In this regard, the importance of recording both retinol and carotene, niacin and tryptophan intakes is emphasized.

Requirements of vulnerable groups

For all of the vitamins included in this report, there is very little direct evidence relating to the requirements of infants, children and pregnant and lactating women.

Infection and vitamin deficiencies

The role of infection in the etiology of vitamin deficiencies and the possible effect of infection, both chronic and acute, on vitamin requirements need further elucidation.

Nature of the diet and vitamin requirements

The degree to which an alteration of the relative proportions of carbohydrate, protein and fat in the diet can affect the human requirements for the vitamins needs further study.

Vitamins in foods

The availability and utilization by the human of the total amount of a vitamin in a food remains an extremely important question, particularly for niacin and the carotenes. The effects of different methods of food preparation should be further investigated.

Specific problems

The minimum effective dose for prophylactic and therapeutic measures

In areas where clinical deficiency is known to occur, prophylactic tests should be undertaken to establish the minimum preventive dose. In the case of vitamin A, the effects of single or intermittent large doses of retinol should be appraised as a prophylactic measure; such dosing might be undertaken during pregnancy, during lactation and/or during the preschool years, with the object of building up liver stores. In areas where mild deficiencies (e.g., night blindness) are encountered, it would be of value to attempt therapeutic tests to establish the minimum therapeutic dose. Such information would help to create at least "minimum requirements" and would be of importance in establishing the "conversion efficiency" of β-carotene in the human.

Protein deficiency and utilization of vitamins

Attempts should be made to clarify the effects of mild protein deficiency on the utilization of retinol and β-carotene; this is of practical importance in the design of preventive programs in many areas. Similarly, further work is needed to ensure the efficiency of conversion of tryptophan to niacin under conditions of low-protein, limited tryptophan

intake; it would serve to establish the relative merits of attempting to increase niacin or tryptophan intakes. In this regard, the importance of amino acid imbalance should also be investigated.

Dietary intake and vitamin A levels in blood and liver

Additional information about vitamin A requirements might be obtained from studies comparing dietary intake with blood and liver vitamin A levels. Data on the accumulation of liver vitamin A stores in exclusively breast-fed infants who have not been given vitamin A supplements would help to build up data to confirm or invalidate the postulated requirement curve (Figure 5).

Water excretory products of retinol

Since various reports of the urinary excretion of radioisotopes derived from labeled vitamin A have appeared in the literature, there is a clear indication of the need for a search for possible water-soluble excretory products of vitamin A in the human. This might be a useful parameter of metabolism and hence of requirement.

Relationship between calorie needs and requirements for thiamine, riboflavine and niacin

More research is needed to establish the relationship between the requirement of thiamine, riboflavine, and niacin and calorie needs. The correlation at very high and very low levels of calorie consumption should be examined to see if it is as good as has been claimed for the more ordinary ranges of calorie intake.

Tryptophan and niacin in growth

The relationship between tryptophan and niacin during rapid growth and late pregnancy remains to be evaluated; certain indirect evidence suggests that conversion may be more efficient during these periods.

11. GENERAL SUMMARY AND RECOMMENDATIONS

General summary

The background (Chapter 1)

The prevalence of deficiency states with respect to vitamin A, thiamine, riboflavine and niacin is discussed in the light of the clinical evidence. The available information from the food balance sheets and food consumption surveys indicates that levels of consumption of these nutrients in most developing countries are low.

Basic concepts and definitions (Chapter 2)

The estimation of needs of these vitamins is a difficult task owing to the limitations of present knowledge. However, the available information on the intake, absorption and utilization of these vitamins and the results of depletion-repletion studies have provided a basis for arriving at reasonably good estimates.

In order to avoid confusion arising out of the use of different terms in current usage to define vitamin needs, it was considered desirable to use the term "recommended intake," which has been defined in the report as the amount which is "considered sufficient for the maintenance of health in nearly all people."

Vitamin A (Chapter 3)

In this report, the term vitamin A has been used in a generic sense to indicate all vitamin A-active compounds, the term "retinol" being employed for vitamin A_1 alcohol.

The very limited nature of evidence from observations on man and

animals has been recognized. However, it is in general consistent and indicates that the average daily recommended intake for an adult man should be in the vicinity of 750 μg retinol per day. In infants, the vitamin A needs per kilogram of body weight are high and fall during subsequent periods of growth, rapidly at first and then gradually until the adult level is reached. A table of recommended intakes at various ages is included. No adjustments need to be made in this table for body size and physical activity. Needs of pregnancy are also assumed to be met at this level of intake; increased needs for lactation are recognized.

Most human dietaries contain retinol, β-carotene and other vitamin A-active carotenoids in different proportions. Taking into account the absorption and utilization of β-carotene and other active carotenoids, a formula for their conversion into retinol is given in the report. It is recommended that the amounts of retinol and β-carotene be reported separately in all food consumption surveys. Tables of food composition should also contain similar information.

Thiamine, riboflavine and niacin (Chapters 4 to 8)

These three vitamins are related to energy metabolism and hence their needs are expressed in terms of 1,000 calories consumed.

The recommended intakes of thiamine and riboflavine are 0.40 mg and 0.55 mg per 1,000 calories, respectively.

With regard to niacin, allowance has to be made for the conversion into niacin of tryptophan, a normal component of dietary proteins. The recommended intake is therefore expressed as 6.6 niacin equivalents per 1,000 calories; 1 niacin equivalent is equal to either 1 mg niacin or 60 mg tryptophan.

The recommended levels of intake of thiamine, riboflavine and niacin equivalents expressed per 1,000 calories need no further adjustment for body size, physical activity, pregnancy or lactation. This is because the nutritionally balanced diets supplying additional calories needed in these conditions will also supply additional amounts of the three vitamins; also, there is no evidence that the vitamin/calorie ratio requires any alteration to satisfy the needs in these special conditions.

It is a fact that under conditions of adequate lactation, exclusively breast-fed infants grow normally on thiamine/calorie and riboflavine/calorie ratios lower than those considered necessary for the adult. The reasons for this are unknown and require further investigation.

PRACTICAL APPLICATIONS (Chapter 9)

The practical implications of the recommended intakes are discussed with reference to (*a*) assessment of the adequacy of total food supplies and the results of food consumption surveys; (*b*) methods of improving the diets in order to attain levels of recommended intake; and (*c*) public health aspects of meeting the needs of vulnerable groups.

SUGGESTIONS FOR FURTHER RESEARCH (Chapter 10)

Important gaps in present knowledge are recognized. Among the problems on which research is immediately needed are:

(*a*) long-term effects of various levels of vitamin intake on health and nutritional status;

(*b*) effect of infection on vitamin requirements;

(*c*) availability and utilization of total amount of vitamins in food;

(*d*) utilization of retinol and β-carotene and factors influencing it;

(*e*) relationship between vitamin A levels in blood and in liver;

(*f*) relationships between the needs of thiamine, riboflavine and niacin and energy expenditure; and

(*g*) factors influencing conversion of tryptophan to niacin.

Recommendations

The group recognized that the figures provided in its report are tentative and that further research may lead to new recommendations. Nevertheless, the group urged that these recommended intakes be accepted as objectives in programs for nutritional improvement and that steps be taken to try to achieve intakes of thiamine, riboflavine, niacin and vitamin A that approximate to the recommended intakes.

The group again directed attention to the vulnerability of the young child to deficiencies of some, if not all, of these nutrients. It particularly drew attention to the occurrence of keratomalacia as a cause of preventable blindness in children and urged that strong efforts be made to ensure adequate intake of vitamin A prior to and during lactation, and during the early life of the child.

Despite the above emphasis on the vulnerability of the growing child, the group recommended that attention also be directed to the adequacy of nutrient intakes for all age groups, since deficiency diseases such as beriberi, ariboflavinosis and pellagra are still seen in populations in several areas of the world.

Finally, the group deprecated programs which overemphasize the provision of individual nutrients (with certain exceptions such as iodine and fluorine). In particular, it drew attention to the potential harm inherent in the provision of protein supplements, which may stimulate growth and hence increase the requirements for other nutrients, unless due consideration is given to the need for ensuring adequate intakes of other nutrients at the same time.

REQUIREMENTS OF VITAMIN A, THIAMINE, RIBOFLAVINE AND NIACIN

Report of a Joint FAO/WHO Expert Group

ROME, ITALY, 6-17 SEPTEMBER 1965

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Appendix 2

GLOSSARY OF TERMS

Vitamin A

Generic term applied to all compounds having vitamin A activity in biological systems. In the report, when specific quantities are discussed, the chemical terms "retinol," "β-carotene" or the term "vitamin A-active compounds" are employed.

Retinol

Vitamin A_1 alcohol. It is also used in the report to include retinyl esters (vitamin A_1 esters), provided that only the weight of the retinol constituent is considered.

β-carotene

Provitamin A. It is also assumed in the report that other naturally occurring vitamin A-active carotenoids will be included quantitatively on the basis that they have one half of the biological activity of β-carotene.

International Unit (IU)

0.3 μg retinol (0.344 μg retinyl acetate) *or* 0.6 μg of β-carotene.

Utilization efficiency

This term has been applied with reference to β-carotene to describe the relationship of its biological activity (in the human) to that of retinol. As explained in Chapter 3 of this report, 1 μg β-carotene is taken to be equivalent to 0.167 μg retinol.

Niacin

In this report "niacin" is used as a generic term to designate all compounds having the vitamin activity. These include nicotinic acid and nicotinamide, as well as nicotinic acid derived from tryptophan. Although a correction is suggested for the conversion of tryptophan to nicotinic acid (see "niacin equivalent" below), no correction seems necessary for the small difference in molecular weight between nicotinic acid and nicotinamide.

Niacin equivalent

Niacin equivalent = 1 mg niacin or 60 mg tryptophan. If a person consumes a diet which has 60 g protein with an average tryptophan composition of 1.3 percent, and the diet contains 5 mg preformed niacin, the niacin equivalents in the diet may be calculated as follows:

Assuming all the niacin is available, it provides 5 niacin equivalents. The diet also provides 0.780 mg tryptophan, which is equal to 13 niacin equivalents (780/60). Adding 13 to 5 gives the total niacin equivalents in the diet as 18.

Recommended intake

The recommended intake is the amount considered sufficient for the maintenance of health in nearly all people.

The recommended intakes are not expected to cover any additional needs which may result from abnormal conditions such as microbial and parasitic infections, malabsorption syndromes or metabolic abnormalities of genetic or degenerative origin; nor are they intended to be sufficient to meet the requirements of extreme environmental conditions. Furthermore, the recommended intakes are applicable only when the requirements for calories and all other nutrients are fully met.

Appendix 3

AVAILABILITY OF CAROTENE FROM VARIOUS SOURCES

Number of subjects	Source of carotene	Intake mg/day[1]	"Absorbed"[2] percentage of intake	Reference
33 infants	Carotene in oil	36–54	[3]72 (31–95)	126
3 infants	Carotene in oil	0.4–2.6	55 (30–70)	127
1 infant	Carrot meal	3.8	50	
7 infants	Carotene in oil	1.1–1.5	36 (25–40)	128
2 "	Carrot, cooked, mashed	0.9, 1.9	2, 3	
2 "	Carrot, raw, mashed	0.4, 0.8	26, 33	
2 "	Spinach, cooked, mashed	0.3, 0.7	12, 2	
2 "	Spinach, raw, mashed	0.3, 0.4	25, 45	
4 "	Tomato juice	0.26	8 (7–11)	
5 infants	Carotene in oil	6–14	68 (59–81)	129
10 infants	Carrot, cooked, pureed	[4]26.7	60 (46–75)	130
4 children	Carotene in oil	8–15	52 (30–75)	127
1 child	Carrot puree	8	30	
1 "	Carrot meal	38	45	
1 "	Spinach, cooked, minced	5	30	
1 child	Carotene in oil	0.9	52	128
6 children	Sweet potato, cooked, mashed	3.6	28 (5–58)	131
5 children	Carrot, raw, grated	19	less than 5	132
5 "	Above + oil	19	about 25	
4 "	Carotene in oil	28	" 45	
1 adult	Carrot, raw	5.5, 15.5	78,87	133
1 "	Spinach, cooked	2.6	88	
1 "	Above, fat-free diet	2.6	52	

Availability of carotene from various sources (*continued*)

Number of subjects	Source of carotene	Intake mg/day[1]	"Absorbed"[2] percentage of intake	Reference
2 adults	Carotene in oil	1.1	59	134
2 "	Carrots, cooked	5.7	1	
2 "	Spinach, cooked	1.1	6	
2 "	Above + fat	1.7	5	
2 adults	Carrot, raw, finely grated	7.9	21 (20,22)	135
2 "	Carrot, raw, coarse	10	2 (2.3,2.4)	
2 "	Carrot, cooked, cubed	26	4 (1.6,5.4)	
5 adults	Carotene in oil	3	52 (46–56)	136
2 adults	Carotene in oil	2	55 (40,70)	127
2 "	Carrot, puree	11, 14	55 (50,60)	
1 adult	Spinach, minced	2	35	
1 adult	Carrots, raw	20	1	137
1 "	Carrots, cooked	13	19	
1 "	Spinach, raw	32	45	
1 "	Spinach, cooked	33	58	
2 adults	Carotene in oil	1.9–19.6	40 (30–51)	138
3 adults	Carotene in fat	1.6–2.7	38 (35–41)	128
3 adults	Carrot, raw, finely grated	6.7	10 (8–13)	139
3 "	Carrot, raw, blended in oil	7.2	47 (32–50)	
3 adults	Carrots, fresh, raw	8.3	13 (11–15)	140
2 "	Carrots, fresh, cooked	8.6	9 (8,9)	
1 adult	Above + oil	8.6	13	
3 adults	Carrots, stored, raw	7.6–30.3	4 (2–7)	
1 adult	Carrots, stored, cooked	32	1.4	
1 "	Above + oil	8	4	
2 adults	Spinach, fresh	9.6	9 (9,10)	
2 "	Spinach, dried	6.3	7 (7,8)	
1 adult	Above + oil	27	7	
1 "	Above, extracted, in oil	6	45	
2 adults	Beet greens	4.5	8 (5,11)	
1 adult	Above, extracted, in oil	22	46	
5 adults	Carotene in oil or fat	3.1–3.6	73 (69–82)	28
2 "	Carrots, canned, sliced	2.2	24 (16,31)	
4 "	Carrots, cooked, puree	3.0	25 (6–36)	
4 "	Above + fat	3.0	33 (0–60)	
2 "	Carrots, cooked, homogenized	3.0	56 (46,63)	
3 "	Spinach, canned, puree	2.5	41 (28–62)	
2 "	Spinach, canned, homogenized	4.0	43 (35–47)	
3 "	Cabbage, dried, outer leaves	1.9	41 (13–60)	
2 "	As above	3.8	28 (28,27)	

Availability of carotene from various sources (*concluded*)

Number of subjects	Source of carotene	Intake mg/day[1]	"Absorbed"[2] percentage of intake	Reference
3 adults	Carrots, fresh, raw	2.9–6.9	42 (37–46)	141
2 "	Carrots, stored, raw	9.2	43 (36,49)	
3 "	Carrot meal, coarse	6.0–7.5	37 (34–42)	
2 "	Carrot meal, fine	1.2	55 (54,56)	
8 adults	Sweet potato, cooked, mashed	3.5	54 (41–50)	142
1 adult	Carotene in oil	1.7	98	143
1 "	Carrot, cooked	2.6	29	
1 "	Carrot, grated, raw	2.1	21	
1 "	Carrot, grated, cooked	2.1	48	
1 "	Above + fat	2.1	46	
1 "	Pumpkin, strained	0.9	53	
1 "	Above + fat	0.9	66	
1 "	Squash, strained	3.2	35	
1 "	Above + fat	3.2	38	
1 "	Spinach, strained	2.4	33	
1 "	Above + fat	2.5	42	
1 "	Spinach, strained	3.4	37	
1 "	Above + fat	3.2	37	
1 "	Seaweed, dried	2.1	8	

[1] When intakes were expressed in international units, they were recalculated on the basis 1 IU = 0.6 μg β-carotene. In some instances, the methods employed did not differentiate between the various carotenes. — [2] For the present purposes the "absorption" is taken as the difference between intake and fecal content (often corrected for carotene excretion on carotene-free diets); see page 23. — [3] Values in parentheses indicate the reported range. — [4] Value represents total dose administered; number of days not known.

DERIVATION OF THE EQUATION RELATING THE RECOMMENDED INTAKE TO THE SOURCES OF VITAMIN A IN THE DIET

The utilization efficiency of β-carotene[1] is only 0.167 (see page 23). Thus, the β-carotene component of a diet is used less efficiently than the retinol component. The recommended intake may be adjusted to take this into account by applying the following formula:

$$R_{(diet)} = \frac{R_{(retinol)}}{0.167\ k + (1-k)} \qquad (1)$$

where $R_{(diet)}$ = Recommended intake of vitamin A-active compounds as found in the habitual diet

$R_{(retinol)}$ = Recommended intake in terms of retinol

k = Proportion of β-carotene in the diet

$$= \frac{\mu g\ \beta\text{-carotene}}{\mu g\ \beta\text{-carotene} + \mu g\ \text{retinol}}$$

This equation may be derived as follows:

The amount of β-carotene in the recommended intake of vitamin A-active compounds is

$$k\ R_{(diet)} \qquad (2)$$

and the amount of retinol is

$$(1\text{-}k)\ R_{(diet)} \qquad (3)$$

The retinol has full biological activity, but 1 μg β-carotene is equivalent to only 0.167 μg retinol. Therefore, the β-carotene would be equivalent to

$$0.167\ k\ R_{(diet)} \qquad (4)$$

retinol.

Therefore, the total vitamin A activity of the recommended intake of vitamin A-active compounds would be the sum of the retinol component plus 0.167 times the β-carotene component, or

$$0.167\ k\ R_{(diet)} + (1\text{-}k)\ R_{(diet)}$$

which may be rewritten

$$[0.167\ k + (1\text{-}k)]\ R_{(diet)} \qquad (5)$$

but this is equal to the recommended intake of retinol. Therefore,

$$R_{(retinol)} = [0.167\ k + (1\text{-}k)]\ R_{(diet)}$$

and

$$R_{(diet)} = \frac{R_{(retinol)}}{0.167\ k + (1\text{-}k)} \qquad (1)$$

---

[1] β-carotene means provitamin A. It is assumed in this report that other naturally occurring vitamin A-active carotenoids will be included quantitatively on the basis that they have one half of the biological activity of β-carotene.

Appendix 5

CONVERSION OF INTERNATIONAL UNITS (IU) OF VITAMIN A IN FOODS TO RETINOL AND β-CAROTENE

1. Papaya has 425 IU vitamin A value, with 85 percent of β-carotene and 15 percent the other carotenoids[1]

then, it has	425 × 85 percent	=	361 IU of β-carotene
	425 × 15 percent	=	64 IU of other carotenoids
or,	361 × .6	=	217 μg β-carotene
	64 × 1.2	=	76.8 μg other carotenoids
but, 1 μg β-carotene		=	2 μg other carotenoids
therefore	$217 + \frac{76.8}{2}$	=	255 μg β-carotene in papaya

The same result can be obtained by multipying 425 by 0.6

2. A sample of milk has 130 IU of vitamin A value: 70 percent is retinol and 30 percent is β-carotene[1]

then, it has	130 × 70 percent	=	91 IU of retinol
	130 × 30 percent	=	39 IU of β-carotene
and therefore,	91 × .3	=	27.3 μg retinol, and
	39 × .6	=	23.4 μg β-carotene

3. Lean meat has 50 IU of vitamin A per 100 g; 90 percent is retinol and 10 percent is β-carotene[1]

then, it has	50 × 90 percent	=	45 IU of retinol
	50 × 10 percent	=	5 IU of β-carotene
and therefore,	45 × .3	=	13.5 μg retinol
	5 × .6	=	3 μg β-carotene

---

[1] See Appendix 6.

ESTIMATED DISTRIBUTION OF SOURCES OF VITAMIN A ACTIVITY (AS IU) IN VARIOUS FOODS [1]

Source	From retinol[2]	β-carotene	Other carotenoids
ANIMAL ORIGIN			
Meat and meat organs	90	10	
Poultry	70	30	
Fish and shellfish	90	10	
Eggs	70	30	
Milk and milk products	70	30	
Animal or fish oil	90	10	
PLANT ORIGIN			
Cereals			
Maize, yellow		40	60
Others		50	50
Legumes and seeds		50	50
Vegetables			
Green vegetables		75	25
Deep yellow (carrots, sweet potatoes - deep orange type, etc.)		85	15
Sweet potatoes - pale type		50	50
Other vegetables		50	50
Fruits			
Deep yellow (apricot, sapote, etc.)		85	15
Other fruits		75	25
Vegetable oils			
Red palm oil		65	35
Other vegetable or seed oils		50	50

[1] From INCAP/ICNND, *Food composition tables for use in Latin America* (1961). For application of this information see Appendix 5. — [2] Including that derived from retinyl esters.

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